

Endocrinology

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January, 1922

A SPONTANEOUS ATTACK OF TETANY DURING A PAROXYSM OF HYPERPNOEA IN A PSYCHO- NEUROTIC PATIENT CONVALESCENT FROM EPIDEMIC ENCEPHALITIS *

(One figure in text)

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The patient, a young man 18 years of age, first came under our observation on February 4, 1921. The chief complaints were "hard breathing," "difficulty in sleeping," and "shipping spells" during which he loses control of himself for five or ten minutes and has only a faint recollection afterwards of what has happened. During the "spells" he talks a great deal, knows that he is talking excessively, but "has no control" over himself.

Family History The father is living (age, 65) and in good health except for occasional indigestion. The mother is living (age, 51) and is very nervous and solicitous. The maternal grandmother is also very nervous. The parents have lost three children and the patient is the only surviving child. There is a history of tuberculosis in the mother's family. All of the attention, worry and solicitude of a very nervous mother have been concentrated upon the patient. He sleeps in her room at night and she occasionally arises "to see that he is safe." Any slight deviation from the routine, a late arrival at meals or remaining out a little late at night, throws the family into a panic.

* This case was reported in abstract at the meeting of the Association of American Physicians held in Atlantic City, N J, in May, 1921.

Past History The patient has always been somewhat nervous and rather dependent, especially in the home, but despite the possibilities suggested by the heredity and environment he has seemed to be a fairly healthy and vigorous boy, not of the studious type but fond of athletics and out-door sports

There is a history of diphtheria, measles and tonsillitis Two years ago a large abscess on the left side of the face was incised and healed satisfactorily Three years ago he suffered a slight blow on the head in an automobile accident

His digestion had always been good up to the time of the present illness

There has been occasional nocturia, the patient being compelled to urinate once or twice during the night for years When about 10 years of age, enuresis occurred practically every night for a year or more and then gradually improved This recurred for a time during the present illness

The patient drinks coffee once a day and smokes from 8 to 10 cigarettes each day His work at school had been satisfactory He had expected to enter the State University last year, but was prevented by illness

Present Illness The present illness began on the evening of January 24, 1920, with a severe headache and a chill He was up and about the next day On the day following, while the patient was playing volley ball at the Y M C A, he became greatly excited, accusing another player of cheating He carried his protestations to extremes and had to be removed from the gymnasium and carried home For the 15 days following he was in a condition of acute mania, talking almost incessantly day and night, sitting up in bed and preaching excitedly about things that at that time were of interest in local politics There was complaint of diplopia and there was fever during these two weeks, the temperature rising each day to about 102° F The fever and the delirium gradually ceased but the patient did not recover rapidly He remained in the house, most of the time in bed, and about 5 weeks after his first attack began to suffer from indigestion with much gas This was accompanied, he says, by "something like asthmatic breathing," a very deep, regular and labored respiration occurring in irregular paroxysms He took a great deal of soda and other medicines in the hope of relieving his indigestion In June, an acute appendicitis developed, and at the operation a gangrenous appendix was found and removed

Later, many pimples (acne) appeared on the face A large abscess developed in the region of the left tonsil and was incised In September, 1920, the tonsils and adenoids were removed

During the spring of 1920 there were occasional "mental lapses" in which the patient would talk at random, quite incoherently From July, 1920, until January, 1921, there were no such mental lapses, but 3 occurred during January, of these, 2 lasted for only a few

minutes, but one on the 12th of January lasted for about 3 hours. He realizes the approach of these "lapses." As he expresses it, he "feels himself slipping", he becomes drowsy and weak. He still suffers a great deal from indigestion, constipation is marked and the dyspnoea persists. He describes also what he speaks of as "trembling spells," which occur daily.

He has a large appetite, complains frequently of hunger at night, and has consumed large quantities of milk in addition to his regular meals, so that he has gained about 25 pounds in weight during the past year.

He is very much more nervous than formerly, sleeps poorly, frequently lies in bed and worries about "impossible things." He occasionally walks in his sleep. There is some depression, but there have been no hallucinations nor delusions. He is not fearful nor suspicious and there have been no attacks of morbid anger.

Physical Examination During the recording of the anamnesis there were periods of very deep and labored respiration, the accessory muscles of respiration being brought forcibly into play. The breathing was very deep and regular and did not interfere materially with speech. As a rule such periods lasted for from 2 to 3 minutes. At the beginning of the physical examination, possibly due to the mental diversion, this deep breathing ceased entirely.

The patient is 5 feet 8 inches tall and weighs 160 pounds stripped. He is approximately 5 pounds over his calculated ideal weight and looks rather larger above the waist than below. The posture is good, the spine straight and the movements of the spine are excellent. Station is good with eyes open and with eyes closed. The gait is normal.

The eyes are slightly prominent and the lid slits are a little wider than usual, the left lid slit being wider than the right. There is a slight Dalrymple sign, but von Graefe's sign is negative. The left pupil is a little larger than the right, both are round and react actively to light. The extraocular movements are good in all directions, but there is slight nystagmus in extreme lateral positions of the eyes. There is no diplopia at present.

The face is covered with pimples, there is a small boil on the left side of the chin, and a long scar (following the surgical incision) below the left jaw. There is no tenderness over any of the paranasal sinuses but there is slight nasal obstruction on the right side. Several molar teeth are missing. There are no obviously dead teeth. The gums are in fair condition. The tonsils have been cleanly removed. The throat is slightly reddened. The tongue is of normal size, slightly coated but not tremulous, protruded in the midline. The mucous membranes are of good color. There is no general glandular enlargement.

The thyroid isthmus is palpable but not full. The lateral lobes are not felt. There is slight swaying of the hands but no fine tre-

mor The hands are well shaped, a little large, the lunulae of the nails show very distinctly

Radial pulsations are synchronous, the rate 72, the pulse is regular in force and rhythm and of good volume. The radial wall is not thickened Blood pressure 125/85 The examination of the heart and lungs is negative

The abdomen shows the scar of a surgical incision over the right lower quadrant, but otherwise is natural in appearance The walls are soft There is no tenderness, there are no abnormal masses Liver and spleen are not felt There has been no hiccoughing

The abdominal reflexes are very active, equally so on the two sides There has been no history of muscular twitchings Deep reflexes of the arms are equal on the two sides and moderately exaggerated Knee kicks are slightly exaggerated Babinski sign is negative Feet are cold and moist, slightly cyanotic

Muscular strength is good, and sensations of touch, pain, sense of position are unimpaired There is no ataxia

Ophthalmoscopic examination shows the discs sharply outlined and of good color Physiological cupping is decidedly larger than usual Vessels are of normal size and normally distributed

The external genitalia are normal in appearance There is a tight anal sphincter The prostate is of normal size and not tender

The axillary and pubic hairs are abundant, and normal in distribution except for a transverse rather than triangular crines Trichosis elsewhere is about normal in amount

During the latter half of the examination the paroxysms of deep, forced respiration recurred at intervals With the increased excitement attendant upon the entrance of a consultant the respirations became deeper and more rapid and continued so After several minutes there was marked sweating of the face and of the axillae and fibrillary twitching of the muscles of the left eyelid was observable A few moments later, there was a typical acute attack of tetany (Fig 1) with bilateral carpal spasm, which persisted for 15 or 20 minutes and then gradually passed off It was accompanied by profuse sweating of the face and neck and by subjective numbness of the affected extremities The feet were not involved During the attack there was a Chvostek sign of first degree strongly positive on the right side, not quite so marked on the left. The spasm of the left hand and arm passed off a little earlier than that on the right side A short while after the attack the Pool-Schlesinger leg test (holding the leg extended at the knee and in marked flexion at the hip) failed to bring on spasm of the foot.

NEUROLOGICAL EXAMINATION (Dr H M Thomas) —The patient is a well nourished boy who gives a remarkably good history of his disease Now and then during the interview he will take a number of deep breaths At other times he will talk along with very slight

interruption After the examination began the breathing became more labored

The pulse beats regularly at about 80

Ophthalmic examination showed Right optic nerve,—temporal edge distinct, nasal edge also distinct, physiological cup deep and rather large, veins of normal size, not tortuous, arteries normal, retina not disturbed so far as seen Left optic nerve,—edges distinct, physiological cup deep, veins and arteries normal

The pupils are moderately dilated, they react to light, directly and consensually, and contract during accommodation The visual apertures are about equal

At times, particularly during deep inspiration, there is a tendency for the lids to droop This is more marked on the right than on the left

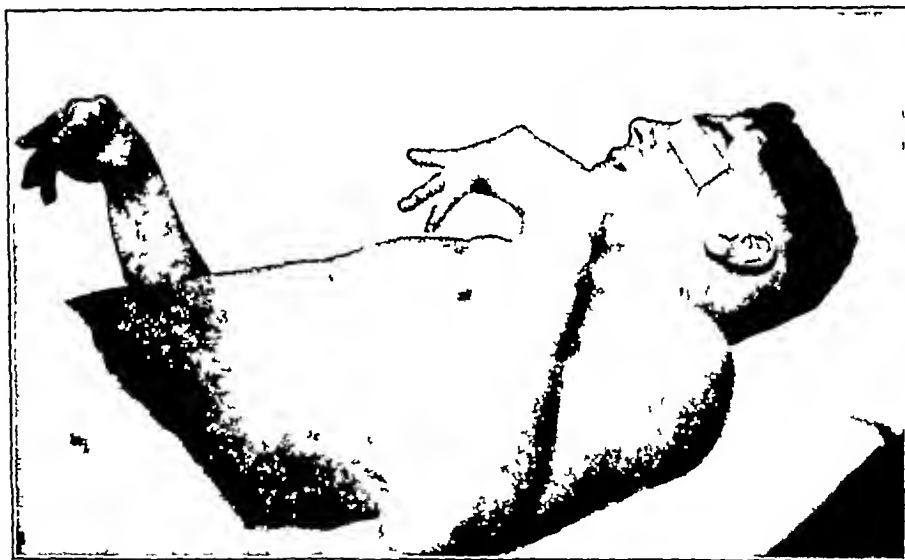


Fig 1 Patient in spontaneous attack of tetany during a paroxysm of pathological hyperpnoea incident to convalescence from epidemic encephalitis (psychotic-ophthalmoplegic type)

The movements of the eyeballs are normal In the extreme lateral positions there are some nystagmoid movements Repeated movements (looking up 20 times) show not the slightest evidence of fatigue

The muscles of mastication act well The jaw jerks is active Sensation on the face is normal

Facial expression is good, except for a slight drooping of the eyes during a dyspneic attack The facial muscles act well and symmetrically Percussion of the branches of the facial nerve does not now produce any unusual muscular contraction

Hearing is normal

The soft palate and tongue act normally

Blood pressure, systolic, ranges now between 115 and 120 When pressure of the cuff is maintained at over 200 for over a minute, there is no tendency to spasm

There is no tremor of the hand The thumb-finger test is done very rapidly There is no ataxia, muscular strength is good, no muscular twitchings are noted

The biceps and triceps reflexes are hyperactive

The abdominal reflexes present and equal

The knee-heel test is done well on both sides Muscular strength is normal No muscular twitchings are noted

Knee jerks are present, slightly hyperactive Ankle jerks are present, slightly hyperactive and equal, no clonus is obtained

On plantar stimulation there is practically no response What there is, shows that the great toe moves in plantar flexion This is also true on descending tibial and sub-malleolar stimulation

No objective sensory disturbance is discovered

Electrical Examination Right ulnar nerve, stimulated above elbow, gives cathode closure contraction at $1\frac{1}{2}$ milliamperes, anodal opening at $1\frac{1}{2}$, anodal closure at 3, cathodal opening not obtained at 5, nor is there a sustained tetanus with cathodal closure Cathodal opening contraction is not obtained with any strength of stimulus

Comment The patient gives an interesting history of what must have been encephalitis, and I am inclined to regard his deep breathing, which is very like some cases of what I have taken to be hysterical breathing, as a functional hang-over from the infection He is the only child remaining and his mother has evidently watched him with great anxiety The curious attacks that he has, which suggest *petit mal*, may be an evidence of anatomical change. I was entirely unable to get any evidence of tetany, and a loss of consciousness in tetany is certainly unusual, except in attacks of extreme severity

PSYCHIATRIC EXAMINATION (Dr Richards) The patient's mental picture during the onset of the acute illness in January, 1920, seems to have been a frank delirium Following this, he was in bed most of the time for two months in a rather dull, inert condition During this time he had no special complaints except those of gas, distention and the sighing reaction which he now shows He thinks the gastrointestinal symptoms have been improved since his appendectomy in June, 1920 Just now he complains of a vague nervous state in which he is easily upset by trifles and sometimes has trembling and jerking attacks During the daytime he is much less alert than at night He says that he has been too wide awake to sleep before 1 a m Aside from the above statement of mental attitude, the psychiatric examination revealed nothing of importance

He responds to the sensorium tests correctly and without retardation The patient has no association connected with the sighing re-

action which apparently developed during the acute illness. While concentrating during the examination he went for five or ten minutes without this symptom.

The present picture is suggestive of post-encephalitic phenomena arising in a suggestible makeup. There is apparently a good deal of petting and coddling on the part of the parents.

EAR, NOSE AND THROAT EXAMINATION (Dr. H. R. Slack) —
Sinuses There is no tenderness on pressure over the sinuses or mastoids. On illumination the frontals are very large and clear, both antra are clear.

There is no enlargement of the lymph nodes at the angles of the jaw.

Nose There is good breathing space on both sides of the nose. There are no polyps, no pus visible.

Teeth are in good condition.

Tonsils have been removed, some remnants remain on both sides, but they are not apparently infected. The *nasopharynx* is negative.

Larynx The epiglottis is turban-shaped, of the infantile type, the vocal chords are slightly reddened and move normally.

The *ears* are normal.

Impression There is no focus of infection in the nose, throat or ears.

LABORATORY REPORTS — *Report on basal metabolism* Height in centimeters, 175, weight in kilograms, 71.8, body surface in square meters, 1.87, CO₂ eliminated per square meter per hour in grams, first period 10.32, second period 11.59. The examination was made twice on account of the deep breathing which washed out the CO₂ before the test. Both tests he took comfortably. The first test was 22.5 per cent below the expected for the patient's age and sex, and the second was 12.9 per cent below. It is felt that the metabolism would be normal or a little low, were it possible to avoid the deep breathing. The second test was taken very soon after the first and when deep breathing was not present.

Blood examination showed R B C, 4,800,000, hemoglobin, 88%, W B C, 5,000, P M N, 65%, P M E, 0, S M, 25, L M, 10. The blood smear was normal in appearance.

The blood Wassermann reaction was negative.

The non-protein nitrogen of the blood was 27.2 milligrams per 100 cc.

Gastric analysis After an Ewald test breakfast, 50 cc were recovered, the contents having a normal gross appearance. There was some mucus present. Free HCl was 50 acidity per cent, total acid, 58 acidity per cent. Tests for occult blood and lactic acid were negative. Microscopically there were many yeast cells, a small amount of starch, but no sarcinae nor Oppler-Boas bacilli.

Examination of the *feces* was negative.

Urine Reaction was acid, specific gravity, 1018-1008 There was a faint persistent trace of albumin in both day and night specimens No sugar, no acetone, no indican were found Microscopically, there were occasional epithelial cells, but no red cells nor casts Phenolsulphonaphthalein test showed first hour, 35%, second hour, 23%, total for the two hours, 58%

Cerebrospinal fluid findings were Fluid clear, 3 cells, globulin negative, Wassermann negative

ROENTGENOSCOPIC REPORTS The lungs and heart are negative The diaphragmatic excursions are satisfactory The retrocardiac space is clear

Fourteen hours after a barium meal there is a thin, wafer-like shadow of retained barium near the pyloric end of the stomach The barium meal fills the colon as far as the splenic flexure, beyond this point the colon is indicated only by its gaseous content. The colon is in good position There is some caecal stasis

At the second barium meal swallowing is normal The stomach is of the cow-horn type, filled without obvious defect, the pylorus lies across the spine and is drawn slightly downward The tonus and mobility of the stomach are good The pylorus is fairly movable

ROENTGENOGRAPHIC REPORTS — *Gastrointestinal tract* The stomach is of the cow-horn type, sluggish in appearance, showing very little peristalsis, the pyloric end of the stomach is blunt and there is no more than a suggestion of a duodenal cap There is a little barium remaining in the stomach 14 hours after the first meal In this series, however, the stomach is empty 5 hours after the second meal There are no definite filling defects noted in the stomach The colon is in good position There is moderate stasis in the caecum, ascending colon and hepatic flexure There is no significant ileal stasis There is a good deal of gas in the colon

Dr F H Baetjer, on examining this series, suspected, however, the existence of an old pyloric ulcer

Lateral skull The sella turcica is smaller than the average and almost closed in The bony outlines are apparently normal The sphenoidal and frontal sinuses are clear The tables of the skull are not remarkable

Paranasal sinuses Frontals and ethmoids are clear, both antra are slightly cloudy, the right more than the left, suggesting an old infection

REARRANGEMENT OF DATA

Young man, aged 18

Chief complaints Hard breathing, insomnia, slipping spells, nervousness

Habits 8 to 10 cigarettes a day

Infections Tonsillitis, diphtheria, an abscess on the face, appendicitis

Operations Appendectomy, tonsillectomy, incision of abscess

Respiratory system X-ray of sinuses shows a slightly cloudy right antrum, evidence of an old infection, special nose and throat examination is negative The lungs are negative There are periods of deep and slightly accelerated breathing, especially on any excitement.

Circulatory system Occasional dyspnoea Pulse rate, 72 Blood pressure 125/85 Heart, normal

Blood and hematopoietic system R B C, 4,800,000, hemoglobin, 88, W B C, 5,000, Wassermann reaction, negative, polymorphonuclear neutrophils, 65%, eosinophils, 0, small mononuclears, 25%

Digestive system Free hydrochloric acid, 50 acidity per cent, total acid, 58 acidity per cent. No occult blood Stool, normal No digestive symptoms until present illness Since then a gangrenous appendix, operation with drainage, constipation, gas, occasional pain in left side, physical examination of abdomen now negative X-rays 14-hour gastric retention, but in this series no 5-hour retention after second meal, caecal stasis, possibility of an old pyloric ulcer Teeth in good condition

Urogenital system Urine Specific gravity varies from 1008 to 1018 A faint trace of albumin No sugar, no casts nor other abnormal elements External genitalia normal Phthalein excretion, 58% in two hours Non-protein nitrogen of the blood, 27.2 mg per cent

Locomotor system Negative

Nervous system and sense organs Always nervous Only child of solicitous parents Acute illness in January, 1920, with fever, diplopia and maniacal delirium for two weeks Residuals Increased nervousness, periods of very deep breathing, lethargy during the day and nervousness and insomnia at night, trembling spells, occasional lapses into slightly manic state with partial amnesia Neurological examination negative for signs of organic disease, possibility of residual *petit mal* attacks Psychiatric examination suggests post-encephalitic phenomena in a person of suggestible makeup Cerebrospinal fluid normal

Metabolism and endocrine system Slightly overweight (five pounds) There was a gain of about twenty-five pounds with the present illness Looks large above the waist There are slight hyperthyroid eye signs Hands rather large Sella turcica small and nearly closed in The basal metabolism was difficult to determine owing to the deep breathing The figures read low, but it was supposed that the metabolism would prove normal or a little low if the deep breathing could be avoided

Remarks There was a typical attack of tetany with bilateral carpal spasm while under observation, apparently resulting from prolonged hyperpnoea Later, during the course of the study, there was no increased electrical excitability of the motor nerves and no evidence of latent tetany could be discovered

DIAGNOSTIC SUMMARY

- 1 Post-encephalitic state, with *petit mal* attacks, functional paroxysmal hyperpnoea and a single spontaneous attack of tetany
- 2 Right-sided abdominal adhesions with caecal stasis, constipation and gastric hyperacidity, suspect pylorus
- 3 A mild endocrinopathy

THERAPEUTIC SUMMARY

The therapy advised in this case included

- 1 A thorough rest and upbuilding treatment with isolation away from home and family, with occupational therapy and psychotherapy
- 2 A change in the diet with diminution in the amount of carbohydrates and especially of milk, which the patient had been drinking in large amounts. The diet recommended included emphasis upon fruits and green vegetables, and moderate amounts of meat, with smaller amounts of easily digested carbohydrates and fats
- 3 For the caecal stasis and constipation mineral oil, one ounce at night and one-half an ounce in the morning. During the period of observation of ten days the bowel functions were apparently very satisfactorily regulated by the use of mineral oil alone. The patient had been in the habit of taking cascara every night and frequently compound cathartic pills in addition
- 4 The gastric hyperacidity was to be combatted by means of an antacid powder after meals
- 5 The right side of the abdomen and the nervous system were to be kept under close observation

The patient did not remain long under our direct observation, but went home after a period of about ten days, taking our report to his home physician. He had been assured that the hyperpnoea was, in our opinion, of functional origin and that it would disappear. He was rather anxious to go home and was kept in a state of suspense for three or four days before this decision was made. His hyperpnoea would occur on any slight excitement during our observation of the case, but never to the extent present at the first examination.

A letter from the patient four or five days after his departure stated that he had not been troubled a single time with his breathing since his return home and that he was feeling fine. This was corroborated a few days later by a letter from his father, who wrote that he had been entirely free from the labored breathing and was more nearly normal than he had been since January, 1920. He came under our observation again several months later. His condition had continued to be fairly satisfactory until June, when there was a return of the insomnia and restlessness at night with increased nervousness and depression. When especially nervous and afflicted with the hyperpnoea he had at times experienced some numbness and a feeling of stiffness in the hands, but there had occurred no outspoken attack of tetany. During a period of rest and upbuilding, with complete isolation, he

soon became comfortable and entirely free from symptoms. On resuming a more natural life there were some neurotic manifestations, but the nervous state in general showed great improvement.

DISCUSSION

This case presents a number of interesting features. It adds another to the already long list of cases of epidemic encephalitis in which maniacal symptoms predominate at the onset. It illustrates, too, a point which has been previously noted, that patients with a psychopathic trend and environment are apt to show marked psychoneurotic residues after an attack of encephalitis. The rapid improvement, also, after a brief period away from home and strong reassurance, was striking and encouraging.

The feature that interested us particularly, however, was the occurrence of an acute attack of tetany during our first examination. The cause of this attack of tetany seemed fairly obvious, but would have been difficult to understand had it not been for the recent experimental physiological studies of Collip and Backus and of Grant and Goldman. These observers showed that tetany regularly occurs as a feature of voluntary prolonged hyperpnoea, probably as a result of disturbed acid-base equilibrium in the body. The observations of the experimentally-produced tetany were made apparently quite independently in the two laboratories, and somewhat similar observations have been recorded by previous workers who did not, however, recognize their significance.

Having the tetany particularly in mind, Grant and Goldman conducted a series of about twenty experiments and were able to produce tetany in each instance after the deep breathing at the rate of about twelve per minute had been continued for from thirteen to seventeen minutes. Their experiments were carefully controlled on the chemical side and the tetany was found to occur after decided changes had taken place in the alveolar air, in the blood and in the urine. The alveolar carbon dioxide tension fell, the blood became slightly more alkaline, the urine became decidedly alkaline, the plasma bicarbonate was reduced, the ammonia excretion was diminished, and there was a slight increase in the calcium content of the blood.

One of their experiments might be detailed as follows. After ten minutes of the deep breathing there was slight headache, after

thirteen minutes tingling in the hands, after sixteen minutes a positive Trousseau sign and a slight Chvostek sign, after seventeen minutes both hands tingled markedly, at twenty minutes a spasm of both hands, at twenty-three minutes spasm of the feet, there was no facial spasm. Twenty-one minutes after the beginning of the experiment the alveolar carbon dioxide tension was 20 mm, having been 40 mm at the beginning of the experiment. At twenty-two minutes after the onset of the breathing the blood pH was equal to 7.5 instead of 7.4, as it was at the beginning of the experiment. The plasma bicarbonate was 45.85%, having been 63.6% at the beginning of the experiment. The urine collected twenty-five minutes after the onset of the hyperpnoea showed a pH 7.9, a change from 4.9 before the hyperpnoea.

The subjects of these experiments were presumably normal men who showed no evidences of latent tetany. The physiologists controlled their experiments to show that food had no influence. Further, they proved that deep breathing itself had no effect, provided the carbon dioxide tension of the alveolar air was not lowered, this they controlled by rebreathing carbon dioxide. Their explanation of the chemical changes is that the deep breathing washes out the carbon dioxide from the alveolar air, reduces the blood carbon dioxide and disturbs the ratio between the carbonic acid and the sodium bicarbonate on which the hydrogen-ion concentration of the blood depends. On re-establishing this ratio the sodium bicarbonate passes out of the blood plasma into the tissues and a considerable portion also is excreted by way of the kidneys. Apparently the carbon dioxide can be washed out more rapidly than the sodium bicarbonate is decreased by excretion or otherwise. Consequently a relative alkalosis develops and at the same time there is a reduction of the alkaline reserve due to elimination of the sodium bicarbonate from the body fluid in the effort to maintain constant hydrogen-ion concentration.

Disturbances of acid base equilibrium toward the alkaline side have been noted before in the study of tetany. Wilson, Stearns and Thurlow and Wilson, Stearns and Janney have noted in parathyroidectomized dogs a period of alkalosis just before attacks of tetany occur. They found that the injection of acid or of calcium salts relieved the tetany. They attribute part of the beneficial action of the calcium salts to a relative increase in the acid radicals by this means, the formation of calcium phosphate $\text{Ca}_3(\text{PO}_4)_2$ from the carbonate, thus liberating hydrochloric acid. Further, Howland and Marriott reported three cases of tetany occurring in infants after the administration of sodium bicarbonate. Harrop reported such a case in an adult.

after the administration of sixty grams of sodium bicarbonate Ammonia poisoning also produces similar symptoms

In previous studies upon tetany it has been found that the calcium of the blood is uniformly low and it has been considered that the administration of calcium therapeutically replaced the needed calcium and in this way protected the body from tetany In these physiological experiments in which tetany was produced by hyperpnoea it has been found on the other hand that the calcium of the blood is slightly increased rather than diminished The question was raised, however, by the authors, as to whether this calcium were in available form

The case reported in this paper is, in our opinion, an example of tetany brought about as an acute manifestation of the chemical changes in the body incident to hyperpnoea There is no evidence whatever that the patient suffered from chronic or latent tetany There had been no previous attack and no history suggesting tetany in his infancy or early youth A half an hour before the attack occurred, during an interval between periods of deep breathing, there were no evidences of latent tetany—a negative Trousseau, Chvostek, etc A day or two following this attack there was no electrical hyperexcitability of the peripheral nerves demonstrable This case, as far as we know, is the first one in the literature illustrating the occurrence of tetany as a complication of a hyperpnoea that is the result of disease Dr Fritz Gundrum of California reports by personal communication that he has seen a similar case recently

There has been a decided tendency in recent years to unify our ideas as to the etiology of tetany and to ascribe the most importance to defective functioning of the parathyroid glands It is difficult to bring the hyperpnoea experiments of the physiologists and cases like that here reported into relationship with parathyroid deficiency It seems possible that parathyroid deficiency may ultimately bring about a disturbance of acid-base equilibrium in the body and hence produce tetany, and that hyperpnoea brings this same condition about much more quickly and without the intervention of the parathyroids Or it may be that tetany is a symptom complex, due not to any single etiological factor but to any condition which heightens the irritability of the peripheral nerves Certainly, it has been definitely demonstrated that this disturbance of the acid-base equilibrium

causes a very marked increase in the irritability of the peripheral nerves so that tetany can be very readily produced even in otherwise normal individuals

Active therapeutic measures directed toward the tetany were not necessary in this particular case. When the patient was left with one companion in the room and his excitement quieted down the deep breathing stopped and the tetany disappeared. A few moments later the Pool-Schlesinger leg test showed no tendency to spasm on the part of the feet or leg muscles. Unfortunately, material could not be collected at the time of the attack of tetany for chemical studies.

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HYPOPITUITARISM AND ITS TREATMENT*

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INTRODUCTION

Clinical use of the term hypopituitarism implies recognition of disease pictures dependent primarily at least upon insufficient pituitary secretion. It is certainly convenient both from a diagnostic standpoint and as a basis for therapy to conceive of the hormone disorders of the pituitary as resulting from either an excessive secretion of normal pituitary products or a diminished production of normal hormones. Whether or not this will prove to be scientifically accurate remains for future proof. It is quite conceivable and indeed rather likely that the simple conception of a quantitatively increased or decreased amount of normal hormones will not be the final explanation of the varied and complex clinical pictures that are at present ascribed to pituitary disease. It may well be that these pictures are produced by a changed or what may be termed abnormal secretion and that therefore a more conservative and correct term for these disorders would be dyspituitarism. Accepting for the present the quantitative idea of hypo- and hyper-pituitarism the clinical manifestations in a given case necessarily depend on first, the exact amount of normal secretion lacking or in excess, second, that time in the life-cycle of the patient when this excess or lack originated, and third, the sex of the individual. When chemical investigations will have revealed the actual hormone or hormones of the pituitary and when methods will have been devised that permit of their quantitative estimation in a given individual, then, obviously, a condition will arise where it would be possible to substantiate that an increased or decreased amount of such hormone or hormones will produce this or that clinical complex. On the other hand, if dyspituitarism is found to be the correct expression for pituitary disorders, such chemical hormones will

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not be recovered in their normal formulas but will be found as chemically altered products

The problem, however, is not even as relatively simple as above presented because other complex factors must be added relating to the bilobar, or maybe even trilobar, constitution of the pituitary, that is to say, a clinical syndrome will depend not only upon the age of onset, the sex and the quantitative question of hypo- or hyper-pituitary secretion but also upon whether this is the result of deficiency or excessive secretion of the anterior lobe alone, the posterior lobe alone, or both lobes together or of increase in one and diminution in the other. Before our clinical analyses can be accurate and our therapy precise and appropriate we must be certain as to just what abnormalities result from anterior lobe disease and what from posterior lobe involvement, and perhaps even from pars intermedia. Much investigation and information has accrued, most interesting and plausible, but surely no good can come of any pretense at this time that our knowledge in regard to these matters is in any sense complete or reliable.

We are accustomed to obtain some satisfaction in our clinical diagnoses of pituitary disorders from skiagrams of the skull showing either enlarged or abnormally small sella turcica, but it should not follow that a normal sized sella rules out pituitary disease, nor does it follow that increased secretion necessitates an enlarged gland nor diminished secretion an anatomically small gland. Functional excess or insufficiency can result from a gland of any size whether large, normal, or small. We are all acquainted with instances of unmistakable hyperthyroidism in which goitre in the sense of an enlarged thyroid does not exist. The degree of toxicity in a case of Graves' disease is not related to the size of the thyroid gland. And precisely as the pathological changes in exophthalmic goitre or adenoma can not be correlated with the clinical toxicity or basal metabolism, so likewise the type of pituitary alteration is no index of the hormonal manifestations. It need only be mentioned that a tumor of the pituitary may produce either typical acromegaly or Frohlich's dystrophy adiposo-genitals.

The various clinical pictures ascribed to hypopituitarism have received their proof of pituitary origin from the finding of

pituitary disease at autopsy, from experimental partial hypophysectomies, and to a slight degree, from amelioration of signs and symptoms through specific pituitary substitution therapy

THE HORMONIC MANIFESTATIONS OF HYPOPITUITARISM

The Osseous System Insufficient pituitary secretion produces extraordinary abnormalities in many different portions and systems of the body and as before stated will produce quite different pictures depending upon whether the insufficiency arises in a pre- or post-adolescent stage. In fact, such insufficiency may have its origin prior to birth and it would seem even in the very earliest embryonic state. The osseous system is definitely involved in many cases of hypopituitarism, though perhaps not as strikingly as in the hyper-syndromes, such as gigantism and acromegaly. Certain types of dwarfism therefore may have their origin in insufficient pituitary secretion prior to adolescence and indeed the opposite of acromegaly, namely, acromikria, is sometimes noted, where the end of the nose and the chin and the fingers and toes are pointed instead of blunt. These small, markedly tapering fingers are quite suggestive.

The Subcutaneous Tissue The subcutaneous tissues are very strikingly involved oftentimes and in quite differing manner—that is to say, one may have extreme emaciation as has been sometimes noted both in diabetes insipidus and in almost complete absence of the anterior lobe, or on the contrary extraordinary obesity which would seem to have a characteristic distribution. It would seem that pituitary obesity is predominately girdle obesity, the fat being astonishingly concentrated on the hips, the lower abdomen, and the mons veneris. The neck and shoulders, upper back and the nuchal region, chest, arms and legs for the most part escape this adiposity.

The Skin The skin in hypopituitarism presents interesting changes. It is quite unlike the hypothyroid or myxedematous. It may be somewhat thick, though often it is thin, but it is not rough nor scaly. It is dry and smooth, as a rule, sometimes like the skin of a baby or child. Often it is marble-like in feeling and appearance, rather pale and waxy, and inelastic and lifeless. It is usually quite sensitive to slight trauma, such patients bruising very readily. When questioned they will admit that they frequently discover black-and-blue marks and do not remember any bump that could have caused them. Slight pressure from the thumb on the arm may cause such a discoloration. These patients rarely perspire and one of the first things that they become aware of soon after pituitary therapy is begun, is a new vitality, elasticity, and warmth of the skin. Some authors have remarked upon and indeed published photographs of a type of skin which is very finely wrinkled, dry and somewhat resembling parchment, but I am more inclined to the notion that this type of skin does not originate from pituitary lack but rather from gonadal deficiency. Possibly it may occur in both conditions since these are so frequently interrelated and difficult to separate.

The Hair and Nails The quantity and distribution of the hair is oftentimes markedly altered in hypopituitarism. If the condition arises prior to adolescence, axillary and pubic hair is apt to be scanty, moreover in men the beard and mustache do not develop or only slightly, so that such patients never or very rarely shave. The pubic hair often assumes the characteristics of the opposite sex, that is to say, the male will not have any hair between the symphysis and the umbilicus, the base of the triangle being upward instead of the apex growing up toward the navel, vice versa in the case of the female, with some hair on the upper lip and chin and perhaps on the chest between the breasts, although this hypertrichosis in the female may be due to suprarenal disease. Trophic disturbances may occur in the nails with longitudinal or horizontal ridging termed onychauxis. A typical case of this sort (with photographs) was recently published by Hollandel. I have seen this condition very remarkably exemplified in one case where the origin, however, would seem to have been atrophy of the testicles, rather than hypopituitarism.

The Generative System Among the most important disturbances associated with preadolescent hypopituitarism must be mentioned those affecting the external and internal genitalia and the secondary sex characters. In the female the external genitalia remain quite infantile, while the internal organs are either exceedingly small and rudimentary or almost entirely undeveloped. (One patient, whose photograph is shown (Fig 2), is 45 years of age and has never menstruated. No definite uterus can be palpated though a thickened strand of tissue in the broad ligament may represent such a uterine body.) If the hypopituitarism begins after adolescence, the appearance of the external genitalia will be normal, but the uterus is apt to atrophy, menstruation becoming irregular, several periods in succession being omitted, or actual amenorrhoea develop. The pubic hair may assume a masculine type and the voice may alter to a lower, harsher, masculine tone. Sexual frigidity is likewise apt to occur. When hypopituitarism affects the male prior to adolescence, the penis, testicles, and scrotum remain quite small and infantile like those of a boy of six years. Moreover, the scrotum may hang in deep folds around the base of the penis resembling somewhat the female labia majora. The pubic hair will be scanty or not present at all and if present will show feminine distribution. The voice may remain that of a boy even after adolescence, high-pitched and effeminate. The configuration of the body is often remarkably feminine, the breasts being considerably enlarged, the hips and the curves of the thighs having a shapely female contour, and the mons veneris being quite prominent. Such men may have but little sexual craving, and may progress to actual impotency. The internal genitalia of the male, the prostate and seminal vesicles, have curiously enough attracted little notice. I have attempted to go over the literature somewhat carefully for notes recording the condition of these organs, but with the exception of one instance in which mention was

made that the prostate was small, this phase of genital development appears to have been entirely overlooked. This would seem an extraordinary omission in view of the striking genital hypoplasia consistently recorded. In a recent number of the New York Medical Journal I called attention to this fact and reported briefly the cases of five boys, each one an excellent example of preadolescent hypopituitarism, in three of whom no prostatic tissue whatever could be palpated, and in the other two only an exceedingly diminutive organ. Since this note was made, two more cases have revealed the same condition. This would seem to suggest that the normal development of the prostate depends in part at least upon normal pituitary secretion.

The Metabolism Metabolism is disturbed at times in pituitary disease as evidenced by polyuria and polydipsia, exemplified in striking fashion by diabetes insipidus. Whether or not this condition is always due to pituitary disease is not yet finally established, and if due to pituitary involvement whether resulting from posterior lobe deficiency or pars intermedia is not yet clear. The fact that spectacular relief, even though temporary, results from administration of posterior lobe extracts does not positively prove its pituitary origin. Such argument would be as faulty as insisting that asthma is due to suprarenal disease merely because administration of adrenalin produces immediate temporary relief. Glycosuria and, on the other hand, greatly increased carbohydrate tolerance, is also found not infrequently in pituitary disease. Basal metabolism is predominantly under the control of the thyroid gland and great increase or decrease is usually attributable to disease of that organ. Whether or not the pituitary gland can also derange basal metabolism has not been finally settled, although the findings of some authors notably Tieney and Engelbach suggest that it may occasionally do so. At present most authorities ascribe the metabolic disturbances mentioned above and also adiposity to posterior lobe disease, but it hardly seems to me that this contention has been finally proven. The administration of posterior lobe in large doses by mouth and also hypodermically has not conditioned reduction in weight to any appreciable degree in some of my cases in which the obesity seemed characteristically of the pituitary type. That the anterior lobe may influence metabolism is suggested by the case reported by Roblee a few years ago in which administration of anterior lobe alone resulted gradually in a loss of over fifty pounds.

The Muscular System The muscular system is also influenced by disordered pituitary function. In the earlier stages of gigantism and acromegaly there is often increased strength, endurance and muscular power. Later when hypopituitarism sets in and also in most cases of primary hypopituitarism, muscular weakness and fatigueability are quite marked. Whether this asthenia involving the muscular system and the blood pressure depend upon a secondary involvement of the suprarenals or whether it be purely of pituitary origin is not yet clear.

Miscellaneous Pituitary disease exercises some influence perhaps upon the body temperature, the pulse rate and the blood pressure. In hypopituitarism the temperature is frequently continuously and considerably subnormal. The pulse rate may be quite slow and the blood pressure lower than normal. Hypotension has been frequently mentioned as a characteristic sign of hypopituitarism. I have found it so occasionally, but by no means as frequently as I was led to anticipate from the reports in the literature.

Mental and Emotional Disturbances Finally, it is to be noted that pituitary disease involves the nervous system and more especially the psyche. It is exceedingly rash and unwise* to leap into the domain of endocrinology for explanation of most mental and emotional derangements, but that some relation exists in some instances can hardly be denied. We are all familiar with the high-strung, agitated, frightfully nervous, anxious temperament of the sufferer from Graves' disease. We are likewise familiar with the stupid, listless, dull, apathy and indifference of the patient suffering from myxedema. We are also aware of the profound changes that occur in the male after castration—both in man and in animals—loss of virility, and energy, of aggressiveness, of masculine love of combat. It is reasonable to associate guardedly some peculiar psychical states with pituitary disease when manifested by patients showing other unmistakable evidence of hypophyseal involvement. Tucker, especially, has called attention to what he terms the several pituitary psychoses. It seems probable that occasionally the pituitary may have an etiological role in epilepsy. The complete and amazing relief from epileptic attacks in some instances by administration of pituitary extract warrants such an assumption. The sweeping conclusion, however, attributing a pituitary origin to every case of epilepsy would be quite ridiculous. One hesitates to go so far as to associate mentality with the condition of the pituitary and yet it seems more than coincidental that marked mental retardation is so frequently seen in preadolescent hypopituitarism. Possibly the same cause that produces the hypopituitarism may be responsible for the mental retardation. Binet-Simon tests in many of these children reveal a mental age from three to eight or more years below their actual age and a few instances have been reported in which administration of pituitary to such children over a long period of time has markedly advanced their mental age and in a manner and at a rate which psychiatrists agree would not have occurred under ordinary circumstances. These results can not be finally accepted as yet, but they are at least encouraging and deserve careful scrutiny.

The above alterations in body function and body structure include fairly well the majority of the hormonal disturbances due to pituitary disease. Just which of these signs and symptoms should be ascribed to the anterior lobe and which to the posterior lobe cannot be positively stated at the present time. Some valuable and interesting classifications have been made, notably the recent one of Engelbach. In a gen-

eral way those disturbances that involve the osseous and the genital systems are believed to be of anterior lobe origin, while the disturbances of metabolism depend upon posterior lobe disease. These matters are, however, not definitely settled and, although they form interesting points for discussion, they should be accepted with some circumspection. Cushing, for instance, at one time at least, ascribed the genital disturbances to posterior lobe involvement. Obviously these points are of more than theoretic and academic interest, since the therapy to achieve desired results must be accurate and for this to be possible the precise functions of the three lobes must be clearly understood.

THE SEVERAL TYPES OF HYPOPITUITARISM

Illustrated by case reports and photographs

The signs and symptoms of hypopituitarism just described group themselves most frequently into a few readily recognized syndromes, as follows:

- 1 The Levi-Lorain type of pituitary infantilism
- 2 The well-known Froehlich type of dystrophia adiposogenitalis

- 3 The less frequently recognized Neurath-Cushing variety

Briefly, the Lorain picture is that of skeletal *undergrowth* with genital aplasia but *without* adiposity, the Froehlich, skeletal *undergrowth* with genital aplasia *and* adiposity, Neurath-Cushing, skeletal *overgrowth* with genital aplasia and adiposity. It will be easier perhaps to visualize these clinical pictures by describing and figuring some typical cases.

CASE I LEVI-LORAIN HYPOPITUITARISM

W. R. (Hospital No 7893, O. P. D. No 66695) (Fig 1), boy aged eighteen. The patient's mother had numerous miscarriages, an uncle had catalepsy. The past history was essentially negative, no ordinary diseases of childhood were reported. The tonsils were removed twice at the ages of eight and nine. There were no complaints except underdevelopment physically. The examination showed the boy to be slender, underdeveloped, with muscular and sexual appearance of about ten years, he had high-pitched voice, no secondary sex characters, no hair on face, axillae or pubes, small penis and testes, and only a very small amount of prostatic tissue, barely palpable. The patient passed all the Binet-Simon tests, even adult, without missing one, there was no mental defect. The laboratory findings were: Blood pressure, 118/60, urine, negative, blood picture, normal, blood Wassermann, negative, spinal fluid, negative, Von Pirquet, negative, blood

sugar curve, 03, 224, 127, 076, urine sugar curve, negative, negative, positive, negative, radiograms showed extensive peribronchial thickening and sella turcica somewhat small The patient is under observation and is receiving increasing doses of anterior lobe pituitary

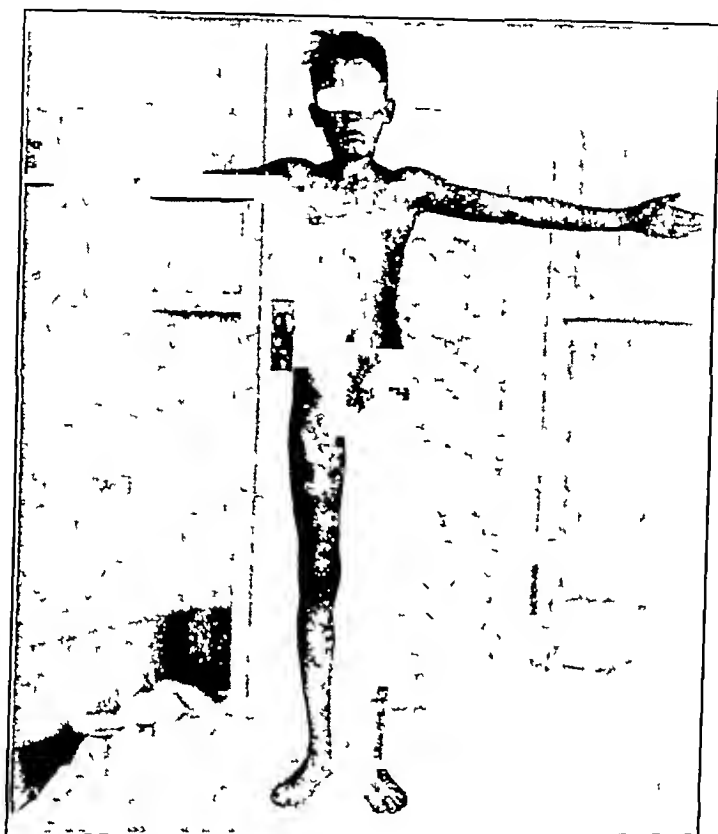


Fig 1 Case I Patient eighteen years old, skeletal undergrowth with infantile genitalia, complete absence of secondary sex characters, sella small Typical case of Loraïn infantilism

CASE II

Miss M McD (Hospital No 9257, O P D No 66375) (Fig 2), is 44 years old She was born and has lived all her life in San Francisco She had measles, scarlet fever, whooping cough in childhood, pneumonia three times recently, acute arthritis recently *She has never menstruated*, has always been severely constipated, always been pale, always cold

Examination shows a small, slender, short woman with peculiar thick, deep, masculine voice, height, 145 cm, upper measurement, 67 cm, lower measurement, 78 cm, skin, dry, thin and wrinkled, hair, plentiful on scalp, but very scanty eyebrows, axillary and pubic hair, saddle nose, expressionless eyes with heavy eye-lids, many wrinkles around eyes and mouth and forehead, facial appearances monkey-like,

thyroid not palpable, breasts practically undeveloped, infantile external genitalia, no uterus palpable rectally, cordlike mass spanning pelvis suggesting rudimentary uterus, small round object size of bean in right broad ligament, probably ovary The blood pressure, is 90/60, urine, negative, blood count indicates marked anemia, Wassermann in blood is negative, spinal fluid, negative, radiograms show a normal sella turcica and epiphyses of hands and feet, joined, sugar curve, normal, basal metabolism, 6% below normal, mental examination, age 9



Fig 2 Case II Patient forty four years old never menstruated Infantile genitalia, cretinoid face with saddle nose, mental age nine years blood pressure 90/60 Case of Loraln infantilism and infantile myxedema

This patient shows pluriglandular deficiency involving pituitary thyroid, ovaries and suprarenals The face is cretinoid but skeletal undergrowth without adiposity and aplasia of the genitalia resembles those of Loraln infantilism

CASE III PREADOLESCENT FRÖHLICH'S HYPOPITUITARISM ASSOCIATED WITH FEEBLEMINDEDNESS AND ABSENCE OF THE PROSTATE

R H, aged 10 years (Fig 3 B) He was one of twins born at full term, he first talked at the age of two and a half years, first walked at three, always was fat and heavy, never played with other children, was good-natured, mentally apathetic, eyes always crossed, could not read, only spoke phrases, no sentences, neither constructive nor

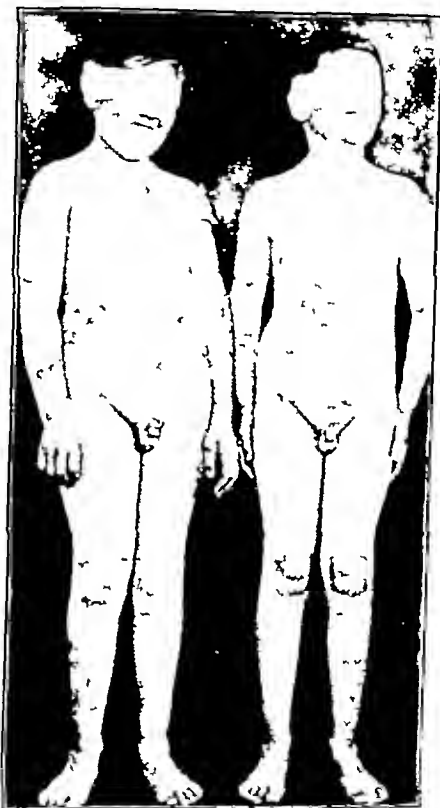


Fig 3 Cases III and IV Twins aged ten Identical examples of Fröhlich's dystrophy adiposo-genitalis Mental age three years, note girdle obesity and infantile genitalia, prostate absent

destructive, had ravenous appetite, was sleepy He had measles, pertussis, pneumonia three times, circumcision, tonsillectomy and adenoidectomy He had large quadrangular skull, coarse dry hair, female contour with broad pelvis, enlarged mammae, marked mons veneris, external genitals of female type with penis in position of enlarged clitoris, no hypospadias, external genitals infantile, no prostate palpable rectally, large feet and pudgy hands with marked muscular hypotonicity, *tache cerebrale*, dermatographia

The mental age was from three to four years, or six years' retardation The laboratory findings were Blood pressure, 118/62, urine, negative, blood picture, negative, Wassermann, negative, Von Pirquet, negative, blood sugar curve, fasting 0.103 per cent, one half hour later

0.129 per cent, one and one-half hours later 0.107 per cent, two and one-half hours later 0.088 per cent, renal sugar curve, negative, eye fundi normal, radioscopy showed normal skull and hands.

This boy and his twin brother (Case 4) are being kept under observation and one is receiving increasing doses of whole gland pituitary extract, while the other is not receiving any treatment, serving as a human control. Their cases will be published some time later in more detail, since in addition to the absence of the prostate, these twins are of extraordinary interest from the fact that they show identical endocrinopathies, suggesting that the pathological factor must have operated in the earliest cell division.

CASE IV PREADOLESCENT FROHLICH'S HYPOPITUITARISM ASSOCIATED WITH FEEBLEMINDEDNESS AND ABSENCE OF THE PROSTATE

W. H., (Hospital No. 7892, O. P. D. No. 67081) (Fig. 3-A), boy, twin, aged 10. The history, physical examination, mental examination and laboratory tests were in every respect precisely similar to the findings of the twin brother (Case III) recorded above, except that the brother was fatter, weighing seven pounds more, and was one inch taller. The figures for the blood sugar curve were 0.116, 0.149, 0.139, 0.106.

CASE V

Private patient, Mrs. L. J. T., aged 28. The family history was negative. She had measles, whooping cough, chicken-pox, diphtheria, scarlet fever in childhood, mumps, at 23, without complications, pleurisy and influenza, menstruation began aged 11, was always very irregular, skipped three and four months at a time until marriage, at 24, then was fairly regular for a year, she then became pregnant, since the baby's birth menstruation has again been irregular and scanty, but the patient claims that two tablets of lutein will bring on a period and produce profuse flow, she is very gloomy and depressed approximately coincidentally with the periods, but at all other times is very jolly. At eleven, just prior to puberty, she weighed 120 pounds, was very stout, at 14 was quite thin, weighing 100 pounds, between 14 and 24, the year of her marriage, she gained steadily, and recently, quite rapidly, to 201 pounds, a gain of 50 pounds in two years. The fat accumulated almost entirely around the hips. The patient is now always sleepy, easily fatigued, has little energy, is usually cold, bruises readily, has no polyuria or polydipsia. Sexual desire and gratification are markedly diminished.

Examination shows height, 5 feet 5½ inches, weight, 201 pounds, fat is principally on hips, skin and hair normal, urine negative, blood pressure 110/80, sella turcica, by radioscopy, small.

Diagnosis Post-adolescent hypopituitarism.

CASE VI

Private patient, Miss M. C., aged 18 years (Fig. 4). Family history was negative. She had measles, mumps, whooping-cough, chicken-pox in childhood, at 2½ years she suddenly became lame in the right leg, the right hip was operated upon in 1915, tonsils and adenoids were removed in 1919, she was always thin until July, 1919. In May, 1919, she weighed 128 pounds, from July, 1919, to October, 1920, she

increased 60 pounds, although she eats sparingly. Menstruation began at 14, was never regular, sometimes came three weeks interval, sometimes five weeks, during 1919 she missed five periods in succession, since July, 1920, she has menstruated but once. She was given thyroid gland by a physician during the early part of 1920, following which, she became very nervous and short of breath, had palpitations, tremor and rapid heart.



Fig 4 Case VI Patient eighteen years old, obesity with amenorrhoea
Fischl's syndrome

Examination Height is 5 feet, 4½ inches, weighs 185 pounds, she is very obese, especially in breasts, hips and abdomen, hair is scanty in axilla and pubic regions, skin is fairly normal, she has rapid, fine tremor, pulse, 120, slight symmetrical enlargement of thyroid with bruit, marked hypotonicity of joints, blood pressure, 145/75, urine normal, basal metabolism 114 per cent above normal,

sella turcica as disclosed by radioscopy, possibly slightly small but maybe within normal limits
Diagnosis Frohlich's syndrome, with therapeutic hyperthyroidism

CASE VII
 Mrs L K, OPD No 72211, aged 37 (Fig 5) Her family history and past history are unimportant. She was married at 16, and has one son, aged 18 years. She has been pregnant but once. Menstruation began at 11, was always regular, every 28 days, flowing rather profusely eight or nine days, until five years ago, when menstruation ceased, at 32. At the age of 23 she weighed 115 pounds, at



Fig 5 Case VII Patient aged thirty seven years menstruation ceased at thirty two sella small marked obesity Post adolescent hypopituitarism
 32, when menstruation ceased, 170 pounds, her present weight is 190. She bruises easily, and is cold most of the time.
Examination She was a short, very fat woman, 5 feet 1 inch in height, weight, 190 pounds, skin of face and arms rough and coarse, big breasts and abdomen, very fat thighs, hair normal, narrow palpebral aperture, uterus and ovaries small, blood pressure, systolic 110, basal metabolism, 55 per cent below normal, calvarium by radioscopy, thick, sella small.
Diagnosis Post-adolescent hypopituitarism with slight hypothyroidism

CASE VIII

Mrs R H, O P D No 68337, 34 years old, negress (Fig 6) Her family history is negative She had measles, mumps and whooping-cough in childhood, pneumonia at 14, typhoid fever at 17, from which she took nine months to recuperate Menstruation began at 14, was regular up to the age of 18, then missed ten months following typhoid

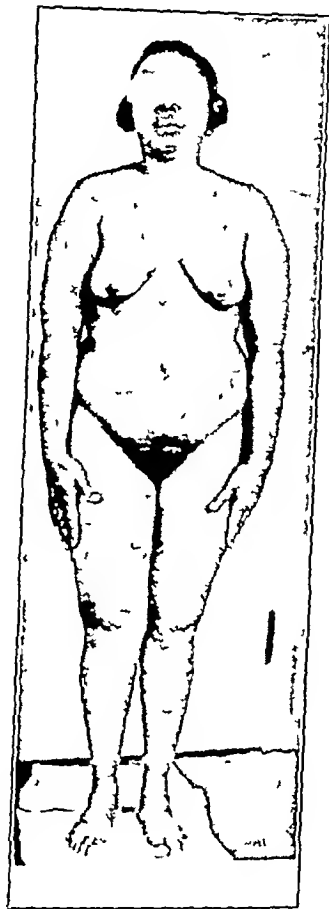


Fig 6 Case VIII Negress aged thirty four obesity and amenorrhoea following typhoid fever small sella, note girdle obesity Post adolescent hypopituitarism

fever, then regular again until 29, then missed for one year without apparent reason, except that she grew very stout at that time, gaining from 150 to 210 pounds, the most she ever weighed She began to menstruate again at 30, and promptly lost 25 pounds, weighing 185, then menstruation was regular until two years ago at 32, there has been no menstruation since that time but the breasts get full and tender each month and she becomes very nervous and emotional with crying spells Sexual desire and gratification are unimpaired She becomes easily fatigued and sleepy

Examination shows "pituitary" obesity, urine normal, flat skull, small sella turcica (by radioscopy)

Diagnosis Frohlich's syndrome, probably following typhoid fever

CASE IX

Mr A C R, private patient, 47 years of age (Fig 7) The father's age was 53, and the mother's 43 when the patient was born One brother shaves very rarely, the other does not shave at all, both brothers are married and have children The patient has two sisters, one is married and has children He had measles and mumps as a child, influenza in 1890, typhoid at 37 He has been married 15 years, the wife is well, there have been no pregnancies In the past four years he has had four peculiar fainting spells usually associated with emotional excitement, there have been no convulsions, he does not bite his tongue or have incontinence of urine or feces

Examination shows weight, 185 pounds, high-pitched voice, cheeks, chin and upper lip entirely devoid of hair (he has never shaved), body

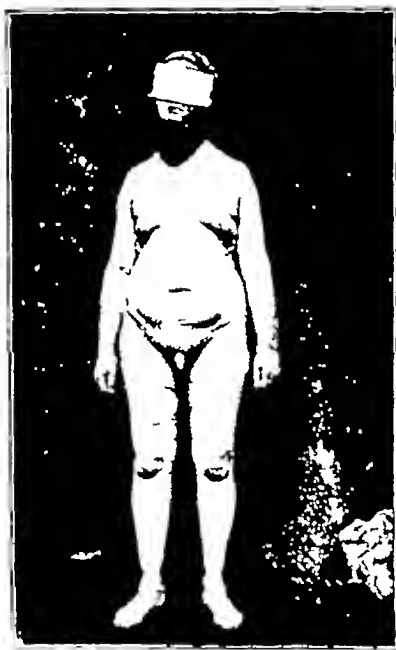


Fig 7 Case IX Man aged forty seven note girdle obesity, feminine configuration marked development of breasts feminine type of pubic hair, infantile genitalia, has never shaved Fröhlich's syndrome

of characteristic feminine contour with abnormally developed breasts, prominent mons veneris and typically feminine hips and thighs, the pubic hair is somewhat scanty and of feminine distribution, axillary hair is very scanty The external genitalia are infantile, resembling those of a boy of eight, the testicles are decidedly small He has never obtained satisfaction from sexual intercourse The skin is dry and never perspires, the thyroid is slightly enlarged He says he had a goitre 12 years ago, which was painted twice a day with iodine and disappeared The blood pressure is 110/75, urine, normal, blood count, normal sella turcica, by radioscopy, small, basal metabolism 26.4 per cent below normal

Diagnosis Fröhlich's syndrome, originating prior to adolescence

CASE X

L Z, O P D No 73098, aged 51 (Fig 8) The father died at 80 The patient's height is 6 feet and the weight 250 pounds No other member of the family, including the mother and four brothers, have any similar disturbances The past history is unimportant The patient noticed that he was different from other boys because they poked fun at him on account of his large breasts and small genitals He has never shaved The voice is high-pitched He has never had any sexual desire or erections or intercourse He was tall for his age and as a boy was fat He was 6 feet tall at 16 years He was always very strong



Fig 8 Case X Man fifty one years old skeletal overgrowth with infantile genitalia Neurath Cushing type of dyspituitarism, never shaved very small prostate

and powerful, being sensitive about not being like other men he always sought very strenuous physical labor, such as that of a sailor, he did deep water diving His case in 1914 was diagnosed by Dr Baiker at Johns Hopkins as "acromegaly and infantilism" At that time he had excruciating headaches with explosive, projectile vomiting Dr Cushing and Dr Horrax of Harvard saw him in 1917 and because of vomiting and headaches decompression was done, apparently a subtemporal—which absolutely relieved the headaches and vomiting almost immediately, he has had none since Drs Rigdon and Stanley performed

transplantation of human testicle into the scrotum in December, 1919. He was demonstrated last year at the California State medical meeting in Santa Barbara. He had several erections within 24 hours following operation, the first he ever had in his life, the transplant did not slough but gradually atrophied, three months following operation he had intercourse successfully twice. There had been no hair whatever on his face prior to the transplantation, but it began to grow about a month later and can be seen in present pictures although he has never shaved—he wants to grow a beard. There has been no hair between the umbilicus and symphysis until recently, there is some present now and also more pubic hair, although he formerly never perspired, the skin has become smooth and moist. While he was with Dr. Barker in 1915, the prostate was searched for and only a very small organ found, for present appearances see figure.

Diagnosis. Neurath-Cushing type—skeletal overgrowth with adiposity and genital infantilism.

The above cases illustrate the principal types of hypopituitarism as they occur both prior to and after adolescence in the male and the female. No partial pictures have been included, such as diabetes insipidus, pituitary psychoses, pituitary epilepsy, pituitary headaches, and pituitary cachexia.

As regards the latter, several cases have been reported in recent years, especially by German clinicians, of extreme emaciation with eventual death, autopsy showing no cause whatever for the condition except extreme atrophy and almost entire absence of the anterior lobe of the pituitary. This would seem to suggest that the anterior lobe can exercise a considerable influence on metabolism, and makes one pause before ascribing the metabolic disturbances to the posterior lobe alone. These findings are, however, very difficult to reconcile with the therapeutic result achieved by Roblee, previously alluded to, in which feeding of the anterior lobe alone, to a subject having Frohlich's syndrome resulted in fifty pounds loss of weight. This matter is briefly mentioned here merely to illustrate the complexity and uncertainty of our knowledge at the present time regarding the functions of the pituitary lobes.

THE ETIOLOGY OF HYPOPITUITARISM

The several varieties above described and illustrated are all the result of pituitary disease. The cause of this pituitary disease is by no means always the same. In the first place, an hereditary factor probably bears some influence in many instances. It is not unusual to discover similar ductless gland disturbances in other members of the family, either in brothers or sisters or in father and mother, uncles and aunts, etc. In such cases we are probably dealing with some defect in the development of the gland. Other instances of hypopituitarism would seem to originate following an acute infectious disease, the infection, as it

were depressing functional activities. A tumor of the pituitary may produce any of the pictures described above. Injuries to the gland either from a foreign body such as a bullet or secondary to fracture of the base of the skull have been reported as responsible for various examples of hypopituitarism and finally lowered pituitary function may be a secondary result of diseases originating in other ductless glands. Injury to the testicles, for example, with consequent atrophy may indirectly result in hypopituitarism as well. An actual infectious disease of the pituitary itself, as syphilis or tuberculosis, may give rise to manifestations of hypopituitarism. Instances have been reported in which anti-luetic treatment of a pituitary gumma has resulted in disappearance or at least marked amelioration of the hormonal disturbance. Probably there are still other causes of hypopituitarism not mentioned above but they may be regarded as somewhat speculative whereas those above recorded have received abundant confirmation.

THE PROGNOSIS OF HYPOPITUITARISM

Obviously this will depend on the nature of the pituitary lesion. If the lesion be a tumor, the treatment becomes a surgical problem, if syphilitic, a matter of anti-luetic treatment, if a congenital lack or if post-infectious, then the treatment will be that of organotherapy. And until this therapy has advanced considerably beyond its present status the prognosis will be exceedingly uncertain. It is equally apparent that the outlook will depend upon the degree to which the hypopituitarism has advanced, which includes both the number of years after onset and the actual age of the patient when seen. Some of the signs and symptoms will be more susceptible to treatment than others.

In a general way the chances of restoring normal function will be brighter (in a case of preadolescent hypopituitarism) if the condition is recognized and treatment undertaken prior to puberty, since the likelihood of developing normal external and internal genitalia is decidedly less favorable after adolescence has once passed by. Early diagnosis and long continued treatment give the best hopes for recovery.

THE TREATMENT OF HYPOPITUITARISM

Let us dispose first of those cases that are due to tumor. Once the diagnosis of neoplasm has been made such patients should be

promptly reported to the surgeon for removal of the growth if possible and otherwise for decompression. Whether after removal or decompression pituitary therapy should be instituted to substitute for whatever glandular lack there may be is a question to decide in each individual case. It does not seem unreasonable to suggest, however, that such additional treatment might occasionally be of value.

Possibly it would be wise in most cases of hypopituitarism to search for and remove foci of infection such as infected tonsils and apical tooth abscesses, etc. This is mentioned because it would seem as reasonable to do so in hypopituitarism as it has become customary to do so in hyperthyroidism. The assumption for such a procedure is naturally based upon the idea that the absorption of toxic products from infectious foci may at times either excite or depress hormonal activity. Proper conservatism is, however, advisable.

We may now properly consider the subject of specific pituitary organotherapy. At the outset it seems to me only fair to state quite frankly that we are still floating about somewhat hesitatingly in what is largely an uncharted sea. Organotherapy is our latest fad in medicine. At times pituitary therapy gives brilliant and most gratifying results. Often it is extremely uncertain if not positively absurd. Judicious conservatism and scrupulous honesty are indeed most urgently needed but often lamentably lacking. The superficial enthusiasm now so rampant will not aid us in finding our landmarks and in charting our way,—rather do they serve to bring the entire subject into disrepute. In the first place, we have no adequate ideas of dosage, none comparable with those that guide us in administering thyroid extract. For instance, shall we prescribe one grain of anterior lobe, let us say, three times a day, ten grains three times a day, as Roblee did, or one hundred grains three times a day, as has Cushing. The careful clinician has many signs and symptoms at his disposal which can guide him in estimating the dosage of thyroid extract. No such criteria have as yet been discovered in the case of the pituitary. We may pour in tablets or capsules in large doses without any particular notion of whether we are benefiting or harming our patient. This is not invariably the case but it happens with sufficient frequency to make pituitary therapy quite uncertain, at times bewildering and often disap-

pointing It is only fair to state that Englebach has suggested control of posterior lobe administration by fixing the dosage at that amount at which the patient has intestinal cramps and diarrhoea about fifteen minutes after injection This may prove to be a helpful index but as yet it is the only method of control suggested How meagre this is when compared to the many toxic signs of overdosage from thyroid—such as tachycardia, tremor, sweating, diarrhoea, loss of weight, nervousness, bruit, eye signs and increased basal metabolism

In particular it should be noted that the literature is rather unsatisfactory, often quite superficial and fragmentary One may find numerous statements to the effect that "under pituitary therapy improvement was noted," but rarely any painstaking details regarding the exact dosage administered, the duration of the treatment, the particular commercial brand used nor the form in which it was given, whether tablet, powder or liquid, and whether by mouth or by hypodermic injection The greatest need at the present time is the recording in a straightforward, scientific manner of many cases treated over a long period of time The haphazard use of pluriglandular formulas although plausibly recommended and occasionally beneficial will not yield in the long run that type of accurate clinical information that is so urgently needed in ductless gland therapy I have already indicated that our knowledge of the specific functions of the anterior and posterior lobes and pars intermedia of the gland is neither complete nor irrefutable We can not be sure therefore whether the products of the posterior lobe or the anterior lobe are indicated in an individual case The solution of lumping them together so as not to miss the one that is needed will not help us in the future to be more accurate and if these products are powerful we may actually be mixing a little harm with a little good Surely then if administration of bilobar products involves a degree of uncertainty in interpreting results, how much more confusing and complex do we make our problem by the addition of two or three gland extracts simultaneously, even though we know that the corresponding glands may be partly at fault Under these circumstances it would seem more prudent to prescribe one gland and preferably one lobe at a time and for a long enough time and in gradually increasing dosage so that one may arrive at a definite opinion as to what has been accomplished in a given

case If the results have been satisfactory well and good, if not, then it is time to begin with another extract and observe its effects Only in this way it seems to me can we follow in reasonably precise manner what we are attempting to do Even then we are confronted with the perplexities that surround all medical administration We should be frank about the brand of preparation used, not with the idea of advertising it if successful or condemning it if disappointed, but because different firms manufacture by different methods Moreover, the dosage of different firms is not always equivalent,—for example, one grain of Burroughs and Wellcomb's organic extracts does not correspond with one grain of Armour's or of Parke-Davis Whether the uncertain results of pituitary therapy are due to methods of manufacture or whether the hormones present in the finished products are at times destroyed or altered in the stomach and not properly absorbed is not yet clear, but whatever the explanation, on the whole the results of pituitary administration are by no means as satisfactory as the results from administration of thyroid extract

It is not my intention to leave the impression that pituitary therapy is always disappointing, rather would I repeat that it is as yet somewhat uncertain Brilliant results of the most gratifying character occasionally reward one, but why success attends its administration in one case and comparative failure in another is difficult to explain One should not place too much confidence in subjective improvement as reported by the patient On the other hand, it would not be fair to disregard this feature of our therapy entirely Patients frequently report more energy, more strength, less sleepiness, and other encouraging symptoms of improvement, but we should be more influenced by objective phenomena such as loss or gain of weight, redistribution of fat, changes in mensuration, growth of body hair, return of menstruation, or sexual potency, pregnancy, changes in temperature and blood pressure and improvement in mental age as indicated by Binet-Simon tests—it being understood that the latter are computed by the same observer in any given case, if possible

In conclusion let me report very briefly a few personal experiences of cases observed sufficiently long perhaps to warrant mention at this time

The boy of eighteen with Lorain infantilism (Case 1) has received pituitary anterior lobe extract. Treatment was begun September 3, 1920, and has continued until March 4, 1921, or six months. At first one grain of B & W anterior lobe pituitary extract twice a day was given. This was gradually increased until he was taking twelve grains daily. After four months a change was made to Armour's anterior lobe pituitary of which he took six grains daily equivalent to about thirty grains a day of the B & W preparation. During this six months there was absolutely no change in the patient's appearance, particularly no development of the genitalia or secondary sex characters. There was no increased growth of hair nor did his voice begin to change to a lower pitch. He grew one inch and a half during this six months and gained seven and a half pounds. This was the only result noticeable and whether this gain in weight and growth of one and a half inches is justly attributable to the pituitary he received or would have occurred in the normal course of events is open to question, although it may be noted that he had remained for two years prior to the beginning of treatment at exactly the same weight. During the last month of observation he received four injections in addition of antuitrin, a liquid extract of the anterior lobe recently introduced by Parke-Davis. If Lorain infantilism is a pure anterior lobe deficiency as suggested by Engelbach, then pure anterior lobe feeding is the therapy indicated. Possibly the above dosage has been too small, possibly if circumstances were different permitting daily injections of antuitrin better results might be achieved.

The twins whose pictures were shown as examples of pre-adolescent dystrophy adiposo-genitalis, on the basis of bilobar deficiency were given increasing doses of whole gland pituitary extract. They have been under observation for almost eight months, taking the medicine steadily and receiving as high as thirty grains a day of B & W pituitary substance. Possibly there has been a slight change in redistribution of fat, their abdomens appearing to be less prominent, but in any case the change has not been striking in this regard nor has there been any development of the genitalia. The twins were ten years of age with a mental age of three years when treatment was begun and at the end of five months their mental age had been increased one year—the tests being executed by the same person. However, here again it is only fair to state that during this period

they had been in a special private school for defective children under close personal supervision and instruction by a trained teacher. Whether this change in environment and special instruction has been responsible for their mental improvement or whether the pituitary extract has been a factor is difficult to judge. Unfortunately the simple experiment did not occur to me until it was suggested just recently of giving pituitary to one of the twins and none to the other, using the latter as a control. This has just been started and it is too recent a change to warrant any positive statement at this time, but should prove an interesting therapeutic experiment.

Case V, the married woman, aged 28, who gained 50 pounds in two years following pregnancy and whose obesity was of the girdle type, whose menstruation became irregular and who was very sleepy and easily fatigued, began treatment a month ago. Her dose of whole gland Armour's pituitary has been increased to ten grains daily and during this time she has also received fourteen injections of posterior lobe extract B & W. Subjectively there has been striking improvement. She voluntarily insists that she is far more active and energetic—more cheerful, and no longer sleepy, and has also noticed marked return of sexual desire and gratification. She has lost eight pounds in weight and the chest circumference and breast circumference have been reduced one inch and the hip circumference one and one-half inches. This is an encouraging beginning.

Case VI, single girl aged 18, who gained 60 pounds in the previous year and who has menstruated only once in the past ten months, began treatment seven months ago. She received during the first six months injections of whole gland pituitary extract B & W, six injections of posterior lobe Paiké-Davis and eighteen injections of posterior lobe B & W, and gradually increased amounts of whole gland pituitary—Armour's, up to fifteen grains daily, which dose she took for eight weeks and which is equivalent to about 75 grains a day of the B & W fresh gland. During this time she lost 15 pounds, her bust circumference decreased two inches, waist measure two and a half inches, and hips one inch. Subjectively she felt very marked improvement and her family enthusiastically remark upon the change in her disposition, she being brighter and more cheerful and far more active. However,

no effect was had upon amenorrhea except that one menstrual period occurred after four months' treatment, and lasted four days, which was the longest she ever menstruated. Recently she has been placed on pure anterior lobe therapy, and is now receiving 15 grains a day of Armour's anterior lobe and three injections weekly of Parke-Davis antuitrin. It is too early to report on the results of this change of therapy. The change was made because there was no further loss of weight or return of menstruation other than reported above. One might reasonably claim some improvement in this patient and she herself is very much pleased, but the results are far from brilliant as yet.

(Later note) The anterior lobe medication was increased steadily, and finally for an entire month she received daily injections of antuitrin and 100 grains daily of dried anterior lobe extract (Armour). Absolutely no effect was noted. Menstruation has now remained absent for a year and a half and no further loss of weight occurred.

Case VII, a married woman, aged 37 years, who suffered from complete amenorrhoea for the previous five years was first given thyroid extract. This was administered for three months with no return of menstruation. Anterior lobe (Armour), 15 grains daily, was then begun and the first period in over five years appeared one month later. Thinking she was cured she remained away for three months and discontinued the medicine. She skipped three periods and regained the 20 pounds she had lost. Then she returned for further treatment. For six months past she has taken anterior lobe (Armour) regularly, gradually reducing from 15 grains to 6 grains daily, and has menstruated regularly and copiously. She has lost 25 pounds in weight and 6 inches around her hips. Treatment in her case has been specific and most satisfactory.

Case IX was that of a man aged 47, with typical Frohlich's syndrome originating prior to adolescence, who had never shaved, who had infantile genitalia and typical feminine contour. He was under treatment for one year and has received varying doses of B & W, anterior lobe pituitary up to 30 grains daily. His weight varied, but on the whole diminished hardly any, but there was striking redistribution of his obesity. He formerly wore a number 16 collar, now wears a number 14, his clothes

had to be altered several times, particularly his trousers. He lost two inches in circumference at the level of his breasts, three inches above his breasts, four inches around his hips. There was no change in the appearance of his external genitalia, but a very slight growth of hair appeared on his face and in the pubic region. A great change occurred in the condition of his skin, which was formerly smooth, inelastic, waxy and cold. He now perspires easily and his skin has more resiliency and is thinner. According to the patient and his wife, there has been an extraordinary change in his character. He has far more energy, is no longer sensitive and retiring, but thoroughly enjoys the company of men, has become more sociable. He has more self-confidence, is cheerful, he and his wife have repeatedly told me that many of his friends comment on the striking change in his manner and appearance.

In conclusion we may say that pituitary therapy is at times brilliantly successful, often worth while and encouraging if persisted in long enough, but sometimes rather disappointing. The great hope for the future lies in the identification and isolation of the actual pituitary hormone or hormones and their manufacture synthetically. This is all the more to be desired because if huge doses are found to be necessary to achieve worth while results, we must be aware of the fact that the supply of animal pituitary is, after all, limited and the expense to some patients almost prohibitive. "In this connection it is interesting to note that approximately five pounds of fresh pituitary glands are obtainable from one thousand head of cattle, which quantity when desiccated, is reduced to one pound in weight." In the meantime until these important discoveries materialize, grants of funds that would permit large doses for many months and even years to patients who could be carefully watched might help to advance our results in this branch of therapeutics.

EARLY OBSERVATIONS PERTAINING TO THE HYPOPHYSIS *

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“If no use be made of the labors of past ages the world must always remain in the infancy of knowledge ” This quotation from Dr Samuel Johnson applies well to the study of medicine in general and to the subject under discussion in particular The early literature on the hypophysis contains much that is speculative, but many important facts concerning the symptomatology and gross pathology were discovered and recorded, and then, unfortunately, passed into oblivion

Owing to the difficulty encountered in collecting and collating these data and separating the important facts from the trivial and useless, one can appreciate the significance of the following statement from Lord Bacon, as paraphrased by Sir Thomas Watson “The lecturer must not be the ant collecting all things indiscriminately from all quarters, as provender for his discourses, nor the spider, seeking no material abroad, but spinning his web of speculative doctrine from within, but rather the bee, extracting crude honey from various flowers, storing it up in the recesses of his brain and submitting it to the operation of his internal faculties, until it be matured and ready for use ”

Possibly the earliest record of a function ascribed to the pituitary appeared in the writings of Galen, who attributed to the gland the power of separating mucus from the brain for secretion

After Galen, in the second century, no contributions were made to the literature until the year 1543, when Vesalius in support of Galen’s view called it the “gland pituitam excipiens” and thought it secreted the mucous discharge of the nose This idea prevailed until 1662 when Schneider disputed the old theory, stating that the nasal secretion did not originate in the pituitary Ten years later Lower in a dissertation on the origin of catarrh supported Schneider’s view

* Read before the Association for the Study of Internal Secretions, Boston, June 6th, 1921

At about this time anatomical studies and case reports with autopsy findings began to appear in the literature Willis as early as 1684 described anatomical changes of the gland, and Bonetus (1700) observed a tumor of the hypophysis Rayer in his article, published in 1823, refers to a number of anatomists, who had observed alterations in the pituitary gland He quotes Wepfer (1734), who described the normal gland and also noted a case in which the gland was twice the normal size Petit (1718), generalizing a small number of anatomical observations, believed that the gland is *squirrheuse* in most individuals affected with hydrocephalus

Morgagni (1766) found that under certain circumstances the glands had a rich yellow color, others were impregnated with considerable mucous material, and again others showed atrophy

Vicq-d'Azyr (1799) mentioned concretions which he observed in the gland substance Bichat in his "anatomie descriptive" also encountered them and found the gland hard and almost scirrhus or in a state of suppuration Chaussier (1812) found in an infant a gland larger than that in normal adults

The report of Rayer's case observed in 1814-15 is interesting, as he describes with great detail a narcoleptic state now recognized as a symptom of advanced hypopituitarism The patient, a man 47 years old, was naturally gay and industrious, but recently had become lazy and extremely careless His ideas were normal and his responses sensible, often thoughtful but slow The memory was impaired and he complained of a feeling of heaviness in the front of the head, which caused him to rub the forehead and eyes mechanically, as one does ordinarily when awaking The vision was impaired He had an insurmountable repugnance for exertion, as getting out of bed On the morning visit he would promise to rise and dress, but after frequent requests from the nurse during the day, at five o'clock he was usually found still in bed If forced to arise he would go to sleep in an arm-chair His attitude was one of extreme weakness, depression and stupor In the evening he dismissed the nurse and went to bed with most of his clothes on, in order, as he said, to avoid the trouble of putting them on the next day Finally he was unable to get up and became completely blind, more depressed and stuporous, incoherent, and eventually pro-

foundly comatosed, when blisters to the back of the neck, mustard poultices to the sole of the feet, julep tonic and decoction of quinine failed to revive him. The autopsy showed very yellow and resistant subcutaneous and omental fat, although not excessive in amount. The hypophysis was much larger than normal, measuring a thumb and a half in diameter, and the tissue was dense and amalgamated with a soft pulpy material. The optic nerve was compressed and flattened at the chiasm.

The above case presents a striking similarity to one observed by Ward in 1823. His patient was a man 38 years old, who suffered from frontal headache, stupor and blindness. He had the same tendency to fall asleep when sitting in a chair, and the headache was severe. Leaches, blood-letting and calomel were resorted to for treatment, but the patient died. The pituitary gland was replaced by a tumor which compressed the optic and olfactory nerves (The London Medical Repository, September, 1823, vol 20, page 217). Based on the records of published cases and his personal observations, Rayer (1823) summed up the knowledge pertaining to the hypophysis at that time in the following deductions:

- 1 Since the uses of the pituitary gland are not understood, its diseases cannot be determined during life by functional disorders
- 2 The pituitary gland is not only altered in structure, but also augmented in size. It compresses more or less the neighboring parts and particularly the optic nerves
- 3 This compression produces phenomena which can make one suspect the seat of the disease, such as pain or heaviness at the anterior part of the head, apathy, impairment of memory, weakness, drowsiness, and blindness, more or less complete, most often in both eyes
- 4 The diseases of the pituitary gland, like those of the parts of the brain situated in the median line, do not cause convulsions or paralysis of one side of the body. The cause, which has produced the development formed by the pituitary, and this tumor itself finally bring about inflammation of the neighboring parts, also symptoms of cerebral phlegmasia at the end of the disease are added to those of compression

- 5 If one cannot hope to be able to distinguish, during the life of the individual, the tumors formed at the expense of the gland and the stem from those developed at the optic chiasm, at least the same difficulties will not present themselves when it is a matter of judging of the diseases of the appendix of the brain compared with those of one of its hemispheres
- 6 The diagnosis of diseases of the gland and of the pituitary "stem" is rendered very obscure by the simultaneous existence of one or several other lesions of the brain

The association of epileptiform seizures with pituitary diseases was probably first mentioned by Raymond Vieussens, 1705 This occurred in the case of "Le cardinal de Bonsy," who died at the age of seventy-two from a tumor of the pituitary gland, the size of a hen's egg For eleven years previous to his death he was subject to convulsive movements, which especially involved the muscles of the eyes, the lips and the tongue, according to the description they were epileptiform in character In addition he developed blindness in the left eye, impairment of intellect, especially memory, and died from an apoplectiform attack

Among other early writers, who mentioned epilepsy in connection with lesions of the pituitary gland, are Greding (1781), who observed anatomical changes in the gland, Wenzel (1810), who observed a tumor and in another case (1811) a reddened and inflamed infundibulum The latter emphasized the fact that the pituitary possesses an important function and suggested the relation of epilepsy to disturbance of this function

Amenorrhea as a symptom of pituitary disease was first mentioned by deHaen in 1761 This occurred in a girl 20 years old She did not menstruate for three months, after which she developed blindness and incessant vomiting, which lasted fourteen days, when the symptoms were relieved by the judicious employment of purgatives Later amenorrhea, vomiting and blindness reappeared, but as purgatives did not relieve her this time, the actual cautery was applied to the left side of the head, which produced an extensive suppurative wound, the patient died in five days from symptoms of meningitis which the author attributed to the effect of the cautery The autopsy presented an un-

usual condition. It showed a left-sided meningitis, the infundibulum was enlarged, measuring 8 or 9 lignes (2 cm) in diameter. It contained pultaceous material and calcareous matter and caused pressure on the chiasm. The blood vessels, especially those distributed to the left hemisphere, contained a large quantity of air. The latter was expressed in italics by Rayer, who cited the case and who further discussed the matter in a footnote. While this observation is purely incidental, it deserves mention because of the possibility of an early recorded case of gas bacillus infection.

Although Morgagni, as early as 1766, has been cited as associating obesity with hypophyseal lesions, the statement could not be verified. However, reference to changes in the color and density of fatty tissue as found at autopsy occur in the early literature of which mention has already been made. Undoubtedly the first authenticated instance of hypophyseal disease with obesity on record is that by Bernard Mohr (1840). He describes a case of fat dystrophy very similar to Frolich's. The patient was a woman 47 years of age, who suffered with disturbance of vision, vertigo, headache, mental deterioration and apoplecticiform attack. Besides, an unusual obesity developed with extraordinarily large abdominal dimensions, especially in the transverse diameter. The autopsy showed a very large degenerated pituitary gland and an enormous amount of subcutaneous fat besides an increase of fatty tissue about the heart, liver and mesentery.

Ocular symptoms are given prominence throughout in the early literature, and the most extensive bibliographies are found in the ophthalmological reviews, thus in Graefe-Saemisch *Handbuch der Augenheilkunde* XI, Band 2, Abt. B, 1915, page 1300-1328, Uthoff gives three hundred and fifty-nine references to articles which appeared in the literature from 1821 to 1901—the period covered in this article—and six hundred and twenty references to 1910, all dealing with ocular manifestations. Amblyopia and amaurosis are frequently mentioned as the chief symptoms in the earlier cases. Later, with improved methods of diagnosis, various ocular disturbances were recognized, most of which are pressure phenomena, including blindness, exophthalmos, abducens paralysis, neuroretinitis, optic atrophy, diplopia, hemianopsia, etc. Blindness the result of tumor of the hypophysis is emphasized by men like Hedlund (1833), Harvey

(1855), and Leber (1866) "The Ophthalmological Society of the United Kingdom" held a very interesting meeting in 1887 (Brit M J, Lond, 1887, Vol 1, p 1334), when a case of optic atrophy in one eye and temporary hemianopsia in the other was reported, and the entire syndrome of dystrophia adiposogenitalis, unrecognized as such, occupied the attention of J B Story, E Nettleship, Dr H Griffith, Dr J Anderson and Dr Coupland, and pituitary lesions in their relation to eye symptoms, obesity, menstrual disturbances and mental manifestations were discussed. Mr Story's case was that of a young woman who gradually became blind in the right eye and had temporal hemianopsia in the left. She suffered with headache, vomiting and irregular menstruation. Her chief complaint was daily drowsiness about noon. During the period of observation it was found that she grew stouter. However, at the time of the report of the case she was able to follow her occupation, her general health being fair. It developed that similar cases were brought to mind and autopsies on them revealed pituitary tumor.

Beginning with the first cases recorded, headache is mentioned as one of the leading symptoms of pituitary disease. It is usually described as occurring in the anterior part of the head and is often paroxysmal in character.

Apparently little or no attention was paid to the genital syndrome until Frohlich associated hypogonitalism with pituitary disease. The anomalies of the secondary sex characters were likewise not recognized.

The year 1886 is significant because of one of the most important contributions to the study of hypophyseal disease by Pierre Marie. The results of his observations were the basis of a thesis which was published under the title of "Two Cases of Acromegaly," an unusual non-congenital hypertrophy of the head and lower extremities in *Revue de Medicine* in 1886 (Paris, 1886, Rev de med, vi, 297-333). This has been translated into English and published by the New Sydenham Society in 1891, vol 87. Marie's essay comprised not only his own cases, but had also reference to a number of others which, unrecognized as a special disease, he had succeeded in finding already recorded in medical literature. The earliest case to which he refers was reported by Sancerotte-Noel. The patient was a man 39 years of age and under observation from 1766-1773, when he died, "after

living too well, from the effects of an overdose of purgative " No autopsy was allowed, but the bones were finally dug up by Sancerotte, and a rib, sternum and clavicle were placed in the Dupuytren museum The author states that the man was obliged to have his hats made for him, having been unable to find any ordinary shape sufficiently large His bones became double their former size The lower jaw measured eighteen inches in length from one condyle to the other, and four inches in depth at the incisors It rested almost on the sternum and gave the patient the appearance of having no neck He was almost always sleepy (a symptom which we now recognize as one of secondary hypopituitarism), which was attributed to the thickness of the skull, causing compression of the brain

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The two monographs of Marie and Souza-Lite furnished such a complete description in respect to the clinical manifestations, skeletal alterations and pathological findings that little knowledge on these phases of the subject has been added since. The chief problem which they left unsolved was the physiology of the gland

The first achievement along this line was the discovery by Oliver and Schafer (1895), who found the pituitary to be a gland of internal secretion, exercising the important function of raising blood pressure, when extract of the whole gland is given intravenously. Howell proved that this peculiar property is present only in the posterior lobe, and furthermore observed that it exerted an inhibiting influence on heart action. During this period of intensive study of the subject it was noticed that the gland is affected during pregnancy—the anterior lobe increasing in size. Rogowitsch (1889) showed that the removal of the thyroid produced hypertrophy of the hypophysis. Then Oppenheim (1899) appears assigning to x-rays an important role in diagnosis, confirming the enlargement of the sella turcica

The recognition of the syndrome described by Frohlich (1901) marked another epoch in the history of the development of the knowledge of pituitary disease. His case was that of a boy 14 years of age with a history of headache and vomiting and rapid increase in weight, the fat distributed in a characteristic manner, the genitalia underdeveloped and the pubic and axillary hair absent (Wien klin Rundschau, 1901, xv, 883-906). A few years later Bartels gave the name *dystrophia adiposogenitalis* to this syndrome. This period represents the dawn of a new era during which remarkable strides have been made through intensive studies by means of methods of experimental research. The result of these investigations led to a clearer conception of the physiology of the gland, and established a basis for the various clinical syndromes produced by an arrested or perverted function

SOME OBSERVATIONS ON WATER AND SALT METABOLISM IN DIABETES MELLITUS

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It is a well known fact that in diabetes mellitus the clinical pictures may be dominated by polyuria and polydipsia. It is also well known that in diabetes insipidus the same symptoms are observed and the question arises whether a relation exists between the two diseases.

This question has been often raised and has given rise to a rather extensive literature. That a relation exists is made probable by certain cases that have been described, in which one disease changed into the other [Senator (1), Lewin (2)]. On the other hand, Naunyn (3) denies any relation between diabetes mellitus and insipidus, and Umber (4) states that it has never been proved that in a case of polyuria and glycosuria a real diabetes insipidus existed. Nevertheless, it is remarkable that patients with diabetes insipidus not seldom give a family history of diabetes mellitus.

Trousseau (5) considered this fact important enough that he prefaced his clinical treatise on polydipsia with the words "Le diabète non sucré peut survenir chez des individus nés de parents qui avaient été polyuriques, glucosuriques ou albuminuriques." Balient (6) described a case of typical diabetes insipidus with hyperglycemia in which a diet free from carbohydrates had a good effect. In some cases of diabetes insipidus in which no glucose is excreted by the kidneys, he advises a determination of the amount of blood-sugar. This is the only way to distinguish between the two diseases.

Teschemacher (7) also believes in a relation between the two diseases and describes some cases in which one form changed into the other. Von Noorden (8), though denying a relation, admits that there have been cases of diabetes mellitus in which, long before glycosuria occurred, marked polyuria with urine of very low specific gravity was seen. He also quotes examples of experimental lesions of the pancreas giving rise to polyuria without glycosuria. Gerhardt (9) and Weber and Grosz (10) be-

At about this time anatomical studies and case reports with autopsy findings began to appear in the literature Willis as early as 1684 described anatomical changes of the gland, and Bonetus (1700) observed a tumor of the hypophysis Rayer in his article, published in 1823, refers to a number of anatomists, who had observed alterations in the pituitary gland He quotes Wepfer (1734), who described the normal gland and also noted a case in which the gland was twice the normal size Petit (1718), generalizing a small number of anatomical observations, believed that the gland is *squarreuse* in most individuals affected with hydrocephalus

Morgagni (1766) found that under certain circumstances the glands had a rich yellow color, others were impregnated with considerable mucous material, and again others showed atrophy

Vicq-d'Azyr (1799) mentioned concretions which he observed in the gland substance Bichat in his "anatomie descriptive" also encountered them and found the gland hard and almost scirrhus or in a state of suppuration Chaussier (1812) found in an infant a gland larger than that in normal adults

The report of Rayer's case observed in 1814-15 is interesting, as he describes with great detail a narcoleptic state now recognized as a symptom of advanced hypopituitarism The patient, a man 47 years old, was naturally gay and industrious, but recently had become lazy and extremely careless His ideas were normal and his responses sensible, often thoughtful but slow The memory was impaired and he complained of a feeling of heaviness in the front of the head, which caused him to rub the forehead and eyes mechanically, as one does ordinarily when awaking The vision was impaired He had an insurmountable repugnance for exertion, as getting out of bed On the morning visit he would promise to rise and dress, but after frequent requests from the nurse during the day, at five o'clock he was usually found still in bed If forced to arise he would go to sleep in an arm-chair His attitude was one of extreme weakness, depression and stupor In the evening he dismissed the nurse and went to bed with most of his clothes on, in order, as he said, to avoid the trouble of putting them on the next day Finally he was unable to get up and became completely blind, more depressed and stuporous, incoherent, and eventually pro-

foundly comatosed, when blisters to the back of the neck, mustard poultices to the sole of the feet, julep tonic and decoction of quinine failed to revive him. The autopsy showed very yellow and resistant subcutaneous and omental fat, although not excessive in amount. The hypophysis was much larger than normal, measuring a thumb and a half in diameter, and the tissue was dense and amalgamated with a soft pulpy material. The optic nerve was compressed and flattened at the chiasm.

The above case presents a striking similarity to one observed by Ward in 1823. His patient was a man 38 years old, who suffered from frontal headache, stupor and blindness. He had the same tendency to fall asleep when sitting in a chair, and the headache was severe. Leaches, blood-letting and calomel were resorted to for treatment, but the patient died. The pituitary gland was replaced by a tumor which compressed the optic and olfactory nerves (The London Medical Repository, September, 1823, vol 20, page 217). Based on the records of published cases and his personal observations, Rayer (1823) summed up the knowledge pertaining to the hypophysis at that time in the following deductions:

- 1 Since the uses of the pituitary gland are not understood, its diseases cannot be determined during life by functional disorders
- 2 The pituitary gland is not only altered in structure, but also augmented in size. It compresses more or less the neighboring parts and particularly the optic nerves
- 3 This compression produces phenomena which can make one suspect the seat of the disease, such as pain or heaviness at the anterior part of the head, apathy, impairment of memory, weakness, drowsiness, and blindness, more or less complete, most often in both eyes
- 4 The diseases of the pituitary gland, like those of the parts of the brain situated in the median line, do not cause convulsions or paralysis of one side of the body. The cause, which has produced the development formed by the pituitary, and this tumor itself finally bring about inflammation of the neighboring parts, also symptoms of cerebral phlegmasia at the end of the disease are added to those of compression

- 5 If one cannot hope to be able to distinguish, during the life of the individual, the tumors formed at the expense of the gland and the stem from those developed at the optic chiasm, at least the same difficulties will not present themselves when it is a matter of judging of the diseases of the appendix of the brain compared with those of one of its hemispheres
- 6 The diagnosis of diseases of the gland and of the pituitary "stem" is rendered very obscure by the simultaneous existence of one or several other lesions of the brain

The association of epileptiform seizures with pituitary diseases was probably first mentioned by Raymond Vieussens, 1705 This occurred in the case of "Le cardinal de Bonsy," who died at the age of seventy-two from a tumor of the pituitary gland, the size of a hen's egg For eleven years previous to his death he was subject to convulsive movements, which especially involved the muscles of the eyes, the lips and the tongue, according to the description they were epileptiform in character In addition he developed blindness in the left eye, impairment of intellect, especially memory, and died from an apoplectiform attack

Among other early writers, who mentioned epilepsy in connection with lesions of the pituitary gland, are Greding (1781), who observed anatomical changes in the gland, Wenzel (1810), who observed a tumor and in another case (1811) a reddened and inflamed infundibulum The latter emphasized the fact that the pituitary possesses an important function and suggested the relation of epilepsy to disturbance of this function

Amenorrhea as a symptom of pituitary disease was first mentioned by deHaen in 1761 This occurred in a girl 20 years old She did not menstruate for three months, after which she developed blindness and incessant vomiting, which lasted fourteen days, when the symptoms were relieved by the judicious employment of purgatives Later amenorrhea, vomiting and blindness reappeared, but as purgatives did not relieve her this time, the actual cautery was applied to the left side of the head, which produced an extensive suppurative wound, the patient died in five days from symptoms of meningitis which the author attributed to the effect of the cautery The autopsy presented an un-

usual condition. It showed a left-sided meningitis, the infundibulum was enlarged, measuring 8 or 9 lignes (2 cm) in diameter. It contained pultaceous material and calcareous matter and caused pressure on the chiasm. The blood vessels, especially those distributed to the left hemisphere, contained a large quantity of air. The latter was expressed in italics by Rayer, who cited the case and who further discussed the matter in a footnote. While this observation is purely incidental, it deserves mention because of the possibility of an early recorded case of gas bacillus infection.

Although Morgagni, as early as 1766, has been cited as associating obesity with hypophyseal lesions, the statement could not be verified. However, reference to changes in the color and density of fatty tissue as found at autopsy occur in the early literature of which mention has already been made. Undoubtedly the first authenticated instance of hypophyseal disease with obesity on record is that by Bernard Mohr (1840). He describes a case of fat dystrophy very similar to Frolich's. The patient was a woman 47 years of age, who suffered with disturbance of vision, vertigo, headache, mental deterioration and apoplecticiform attack. Besides, an unusual obesity developed with extraordinarily large abdominal dimensions, especially in the transverse diameter. The autopsy showed a very large degenerated pituitary gland and an enormous amount of subcutaneous fat besides an increase of fatty tissue about the heart, liver and mesentery.

Ocular symptoms are given prominence throughout in the early literature, and the most extensive bibliographies are found in the ophthalmological reviews, thus in Graefe-Saemisch *Handbuch der Augenheilkunde* XI, Band 2, Abt. B, 1915, page 1300-1328, Uthoff gives three hundred and fifty-nine references to articles which appeared in the literature from 1821 to 1901—the period covered in this article—and six hundred and twenty references to 1910, all dealing with ocular manifestations. Amblyopia and amaurosis are frequently mentioned as the chief symptoms in the earlier cases. Later, with improved methods of diagnosis, various ocular disturbances were recognized, most of which are pressure phenomena, including blindness, exophthalmos, abducens paralysis, neuroretinitis, optic atrophy, diplopia, hemianopsia, etc. Blindness the result of tumor of the hypophysis is emphasized by men like Hedlund (1833), Harvey

(1855), and Leber (1866) "The Ophthalmological Society of the United Kingdom" held a very interesting meeting in 1887 (Brit M J, Lond, 1887, Vol 1, p 1334), when a case of optic atrophy in one eye and temporary hemianopsia in the other was reported, and the entire syndrome of dystrophia adiposogenitalis, unrecognized as such, occupied the attention of J B Story, E Nettleship, Dr H Griffith, Dr J Anderson and Dr Coupland, and pituitary lesions in their relation to eye symptoms, obesity, menstrual disturbances and mental manifestations were discussed Mr Story's case was that of a young woman who gradually became blind in the right eye and had temporal hemianopsia in the left She suffered with headache, vomiting and irregular menstruation Her chief complaint was daily drowsiness about noon During the period of observation it was found that she grew stouter However, at the time of the report of the case she was able to follow her occupation, her general health being fair It developed that similar cases were brought to mind and autopsies on them revealed pituitary tumor

Beginning with the first cases recorded, headache is mentioned as one of the leading symptoms of pituitary disease It is usually described as occurring in the anterior part of the head and is often paroxysmal in character

Apparently little or no attention was paid to the genital syndrome until Frohlich associated hypogenitalism with pituitary disease The anomalies of the secondary sex characters were likewise not recognized

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This question has been often raised and has given rise to a rather extensive literature. That a relation exists is made probable by certain cases that have been described, in which one disease changed into the other [Senator (1), Lewin (2)]. On the other hand, Naunyn (3) denies any relation between diabetes mellitus and insipidus, and Umber (4) states that it has never been proved that in a case of polyuria and glycosuria a real diabetes insipidus existed. Nevertheless, it is remarkable that patients with diabetes insipidus not seldom give a family history of diabetes mellitus.

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lieve that in cases in which both diseases are seen in one family the nervous disposition is hereditary, but that this is no proof that diabetes insipidus and mellitus bear any relation to each other.

If we ask whether a relation between both diseases is "a priori" probable, we must answer that the existence of such a relation may not be considered impossible. Until recently it was generally accepted that the hypophysis played an important part in the pathogenesis of diabetes insipidus. In some cases data given to prove this are not very convincing.

The proofs given by Sekiguchi (11) of the hypophyseal origin of polyuria in cases of carcinoma of the breast are not at all convincing. The same can be said of most publications on the subject [Hoppe-Seyler (12, 13), Newmark (14), Meyenburg and Mason (15), Marañón (16), and others]. Hoppe-Seyler, however, is rather careful in his expressions and admits the existence of a diabetes insipidus without lesions of the hypophysis. A very remarkable case may be mentioned here. Luzzatto (17) reports a case of diabetes insipidus caused by a hemorrhage into the hypophysis. Necropsy disclosed no changes in the brain. Such a case may perhaps prove that in extremely rare instances the hypophysis alone may be the cause of diabetes insipidus. Cushing and Biedl in their monographs suggest that the hypophyseal hormone ascends by the tuber cinereum to act on the proximal mesencephalic centers, and Marañón (18) calls this suggestion very probable. I cannot agree with this. The fact that complete removal of the hypophysis does not cause polyuria affords convincing evidence against this contention. The work of Camus and Roussy (19, 20), of Leschke (21) and of Aschner (23) has proved that lesions of the brain near the tuber cinereum may produce polyuria and diabetes insipidus. Tumors of the hypophysis only give rise to diabetes insipidus when they press on the base of the brain. Anatomically as well as experimentally, the existence of a center for water metabolism near the tuber cinereum has been proved. In the same way the probability of the importance of the hypophysis in the pathogenesis of diabetes mellitus has become smaller and smaller. It has been proved that the so-called hypophyseal diabetes probably has its origin also near the tuber cinereum. The frequent combination of acromegaly with glycosuria does not speak against this.

Loeb (24) had observed as early as 1898 that acromegaly, caused by a tumor of the hypophysis, was only complicated with glucosuria when the tumor had reached a certain size and that when, by some cause or other the tumor became smaller the symptoms of diabetes mellitus disappeared. Loeb rightly concluded that this hypophyseal diabetes was caused by pressure on the third ventricle, a view confirmed by recent investigations.

We have thus a right to believe that if the centre for the water and sugar metabolism near the tuber cinereum are not identical, they are situated close to each other. It is the same with the centre in the fourth ventricle. The pique of Claude Bernard proves this. Claude Bernard knew perfectly well that this operation could produce polyuria as well as glycosuria. The anatomy of the sugar centre shows how complicated these things are. Dresel and Lewy (25) proved that there are sympathetic cells in the pars posterior of the nucleus dorsalis vagus. When they are stimulated they cause sugar mobilization and hyperglycemia. The pars anterior of the nucleus dorsalis vagus contains parasympathetic cells. When they are stimulated the formation of glycogen is increased. Both centres are influenced by a higher centre in the so-called nucleus periventricularis. As mentioned above, the sugar centre in the fourth ventricle must be in close relation to the water centre. It is possible that another sugar centre is situated in the corpus striatum, but too few facts are known to justify a discussion as to whether this has any relation to the water metabolism.

From these statements it may be concluded that a relation between diabetes mellitus and insipidus is not "a priori" absurd. To attain more certainty it is necessary to study the character of the polyuria in both diseases. In diabetes insipidus some authors believe that the kidneys have lost their power of concentration. Whether this is due to a renal lesion or not is of no importance in the present connection.

Whether the polydipsia or the polyuria is the primary condition will not be discussed either. The fact is that large quantities of urine of very low specific gravity are excreted. Different authors disagree as to the mechanism of this process. Umber (1c), Tallquist (26), Erich Meyer (27, 28), Kennaway and Mottram (29), and others state that the concentrating power of the kidney for solids has disappeared.

Golke (30) believes that this is true only for NaCl, and that the effect of pituitrin is due to an increased concentrating power of the kidney for this substance. Lechtwitz and Stromeyer (31) state that sodium chloride cannot be excreted in normal concentration, but nitrogen can, Forschbach and Weber (32) describe a disturbed function of concentration for some substances only. Other authors, however, are of an opposite opinion. Hecht (33) describes a highly interesting case of diabetes insipidus, which was caused as a Heineheimer's reaction after an injection of salvasan in syphilis. From this case and from the literature, he concludes that in diabetes insipidus the function of concentration of the kidneys is absolutely normal. Nicolaysen (34), and Barach (35) also describe a sufficient power of concentration by the kidneys.

Socin (36) observed that all NaCl ingested was quickly excreted, giving rise to an increased diuresis. When the patient was allowed to take as much water as he liked, the amount of chlorine in the blood was normal, if the quantity of water was restricted the rise of the amount of chlorine was enormous—even to 1.03 per cent! Goldberg and Heiz (37) found that the power of concentration was rather good. They were able by giving NaCl to increase the concentration of the urine threefold. Rosenbloom and Price (38) conclude from their work that there are cases in which the renal concentration power is lost and others with a real polydipsia in which this function is normal. How complicated this question is is shown by a highly interesting article of Bauer and Beita Aschner (39). They describe quite a number of mechanisms of diabetes insipidus. One feels inclined no longer to consider diabetes insipidus as a disease entity, but as a symptom of different diseases.

Veil (40) has described two different forms of diabetes insipidus. The first shows an increased quantity of chlorine in the serum, the second hypochloreaemia. Pituitrin has a temporary influence only in cases with hyperchloreaemia. In the other cases pituitrin has no influence whatever. It is a well known clinical fact that there exist cases of "pituitrin-feste" diabetes insipidus, this has been once more specially referred to by Bauer and Aschner (1c). Some other remarkable experimental facts have been discovered by Veil (41). Piqure of the fourth ventricle gives polyuria, hyperchloruria and hypochloreaemia, piqure of

the midbrain is followed by polyuria, hypochloruria and hyperchloræmia

In relation to these different opinions, it must be borne in mind that such work in patients with diabetes insipidus is not always easy, on account of the virtuosity of such patients in stealing water. We may thus conclude that probably there exist at least two types of diabetes insipidus

We may now consider what are the characters of polyuria in diabetes mellitus. Not much literature has been published on this subject. Beard (42) and Beard and Rowntree (43) found that in some cases chlorine may be retained in the serum and that these cases may be complicated by edema. Nelson (44) estimated in a number of cases the excretion of nitrogen, chlorine, calcium and magnesium, but though he found some interesting facts they have no relation to our subject. The books on diabetes generally do not mention these matters. Cammidge (45), who considers them briefly, comes to no conclusion. Allen (46) devotes a short chapter to them, but cites no conclusive data. Frerichs (47) states that in diabetes there is hyperchloruria and that this is due to an increased quantity of chlorine taken by mouth. The only remark I found in the literature in which the question is put in a right way is in a study of Leschke (48). He carried out experiments on the concentration-power in diabetes mellitus with polyuria and came to a belief in a similarity between the excretion of water and salts in diabetes mellitus and diabetes insipidus. However, he devotes only a few words to these experiments.

I have been able in three cases of diabetes mellitus with polyuria to study the excretion of water and salt. Of the *historia morbi* I shall mention only these facts that are of importance as indicating the severity of the cases. The number of cases studied in these experiments is limited to three patients, because it is possible to work only with patients who may be expected not to try to deceive doctor or nurses. If a patient will not be honest the most severe isolation will be useless.

Case I Teacher, 32 years of age. For three years polyuria, polydipsia, and polyphagia have been noted. Urine is frequently passed. When I saw him for the first time his urine contained 9 per cent glucose, much acetone and diacetic acid. After 10 days, "Mehlfruchtekur" acetone had disappeared, diuresis (7 liters) with 4.2 per cent glucose persisted. For 4 days the following diet was given. Bread,

80 gm , milk, $\frac{1}{2}$ liter, veal, 150 gm , 1 egg, 50 gm unsalted butter, 500 gm of spinach or endive This diet resembles that of Forschbach and Weber No salt was added to the vegetables The NaCl content of this diet is about 1-2 gm daily The patient did not protest against this tasteless food It is, if possible, desirable to give this diet for some days since, as has been shown by Borelli and Girardi (49), a NaCl equilibrium is only slowly reached The fifth day every 2 hours (during the day time) the urine was collected, measured and examined The estimations of specific gravity, as found in diabetes insipidus literature, has of course little importance in diabetes mellitus since it is too much altered by the presence of glucose

TABLE 1

Hour	Quantity of Urine (c c)	NaCl in %	NaCl in Gm	Quantity of Water Taken (c c)
8-10	600	0 01	0 06	1000
10-12	850	0 009	0 0765	800
12- 2	720	0 013	0 1236	800
2- 4	800	0 017	0 136	600
4- 6	450	0 008	0 036	700
6- 8	670	0 024	0 1608	400
8-10	380	0 01	0 038	1000
10- 8	2750	0 008	0 2200	1760
	7220		0 8509	7060

The most important conclusion that may be drawn from this table is that the patient is reliable The quantity of water taken and excreted do not show an important difference Some water is also excreted extrarenally The NaCl is partly retained or at least not excreted with the urine This fact became still more obvious on the next day, when with the breakfast 10 gm of salt was given

TABLE 2

Hour	Quantity of Urine (c c)	NaCl in %	NaCl in Gm	Quantity of Water Taken (c c)
8-10	360	0 024	0 0864	400
10-12	580	0 12	0 696	400
12- 2	1020	0 20	2 04	900
2- 4	620	0 22	1 364	700
4- 6	540	0 14	0 756	800
6- 8	620	0 09	0 558	700
8-10	350	0 08	0 280	800
10- 8	2360	0 13	3 068	2000
	6450		8 8484	6700

Here we see that a small part of the NaCl is retained in the body, though it is seen that the kidney has not lost its power of concentration, but that, on the contrary, its concentrating function is excellent

It would have been important to estimate the chlorine content of the blood. This could not have been done every two hours, but was done every day for a week. Bang's micromethod (50) was used

Date	Chlorine in %
12 April	0.61
13 April	0.62
14 April	0.60
15 April	0.63
16 April	0.69 10 gm NaCl
17 April	0.68
18 April	0.63
19 April	0.61

Here we see in first place that even when diet is very poor in salt there is a slight but distinct hyperchloraemia. The influence of 10 gm of NaCl is still seen next day, when the greatest part has been eliminated through the kidneys. If these figures were submitted to one not knowing any clinical details of the case, his diagnosis would probably be "diabetes insipidus with hyperchloraemia."

Case II A colonial officer, 48 years old, was treated in India for diabetes. He came with complaints of polyuria and polydipsia. The urine did not contain acetone or diacetic acid, but 2.4 per cent glucose with a diuresis of 9 liters. In this case the examinations could not be carried out every two hours, but were done with the urine of 24 hours. He received a mixed diabetes diet with 100 gm bread and 6-8 gm of NaCl daily.

TABLE 3

Date	Quantity of Urine (c c)	Chlorine in %	NaCl in Gm	NaCl in Blood	Quantity of Water Taken (c c)	
3 May	8900	0.06	5.25	0.70	9000	10 gm NaCl extra
4 "	9100	0.03	2.73	0.68	8500	
5 "	9470	0.05	4.70	0.69	10000	
6 "	11200	0.06	6.72	0.74	12000	
7 "	10800	0.05	5.40	0.72	11000	
8 "	9000	0.06	4.50	0.70	8550	

Here also we have a case of diabetes with hyperchloraemia. Not much influence is seen from the administration of 10 gm of NaCl on the concentration of the urine. A remarkable fact is seen in the table.

When we know the quantity of NaCl ingested was approximately the same every day (and much attention was paid to this) then on May 3rd, 4th and 5th, 12.68 gm of NaCl was eliminated in the urine, on May 6th, 7th and 8th, 16.62 gm. On the 8th of May, at which date diuresis has reached its ordinary height, the greatest part of the extra NaCl was still retained in the body, not in the blood, as is seen by the amount of NaCl in the serum. We are inclined to believe that it is retained in the tissues.

This corresponds with the theories of Veil (1c), Boenheim (51), and Meyer and Meyer-Bisch (52) on the action of pituitrin. In this case it seemed of some interest to study the influence of pituitrin.

There was no reason to fear its influence on the diabetes mellitus. Not only have some authors recommended the use of hypophysis preparations in diabetes (Vigevani, 53), but diabetes mellitus is not considered as a contraindication for the use of these substances (Borchard, 54). It was observed that pituitrin had a marked influence on the excretion of water.

On May 9th the patient got four injections of 1 c.c. pituitrin.

TABLE 4

Time	Quantity of Urine (c.c.)	NaCl in %	NaCl in Gm	NaCl in Blood	Quantity of Water Taken (c.c.)	
8-10	1080	0.05	0.540	0.69	900	10 o'clock 1 c.c. pituitrin
10-12	360	0.13	0.468	0.68	400	
12-2	220	0.12	0.264	0.69	300	2 o'clock 1 c.c. pituitrin
2-4	150	0.30	0.450	0.66	100	4 o'clock 1 c.c. pituitrin
4-6	0			0.66	300	
6-8	420	0.41	2.722	0.67	300	8 o'clock 1 c.c. pituitrin
8-10	200	0.38	0.76	0.68	150	
10-8	1260	0.24	3.024		1200	
	3690		8.228		3650	

Though the influence of pituitrin is not so enormous as in some cases in the literature, it cannot be denied. It is remarkable that the NaCl content of the blood did not change. It seems to be possible in diabetes insipidus by administration of pituitrin subcutaneously dur-

ing a long time to obtain a temporary anuria (Gorke) and to obtain a normal NaCl content of the serum (Meyer and Meyer Bisch) It takes, however, many days of treatment before this is reached

TABLE 5

Date	Quantity of Urine (c c)	NaCl in %	NaCl in Gm	NaCl in Blood	Quantity of Water Taken (c c)	
8 Sept	4750	0 24	11 400	0 54	5000	
9 "	5380	0 21	11 298	0 57	5450	
10 "	4250	0 22	9 350	0 57	4600	
11 "	6130	0 32	19 616	0 58	7000	10 gm NaCl at breakfast
12 "	4060	0 23	9 338	0 55	4120	

It would have been of interest to study the influence of thirst on metabolism, but as none of my patients could stand the headache they got in trying this, the experiments have not been continued

Case III A military officer presented a very serious case When I saw him for the first time, diuresis was approximately 5 liters daily, with 3.7 per cent glucose, large quantities of acetone and diacetic acid

TABLE 6

Hour	Quantity of Urine (c c)	NaCl in %	NaCl in Gm	NaCl in Blood	Quantity of Water Taken (c c)	
8-10	600	0 21	1 26	0 56	720	10 o'clock 1 c c pituurin
10-12	450	0 23	1 03	0 58	300	
12- 2	400	0 21	0 82	11 56	540	2 o'clock 1 c c pituurin
2- 4	580	0 20	1 16	0 56	430	
4- 6	300	0 23	0 69	0 58	200	6 o'clock 1 c c pituurin 8 o'clock 1 c c pituurin
6- 8	420	0 24	1 01	0 56	700	
8-10	680	0 20	1 36	0 56	420	
10- 8	1260	0 21	2 64	0 56	1400	

He died some months after the onset of treatment in coma diabeticum Here we have quite another type than in the two preceding cases

Here we see a perfectly normal salt and water elimination. The amount of NaCl of the serum is normal, perhaps somewhat low. If we should feel inclined to compare this case to one of diabetes insipidus, it would be the hypochloaemic form. The difference from the normal is, however, too small to justify this diagnosis. Pituitrin had not the slightest influence on salt or water metabolism as is proved by the following data

SUMMARY

There exist cases of diabetes mellitus with polyuria in which water and salt metabolism closely resemble the water and salt metabolism in the hyperchloaemic form of diabetes insipidus. There also exist cases in which such a resemblance cannot be demonstrated. Three case reports with metabolism findings are submitted in substantiation of these conclusions. It is not yet certain whether there exist cases of diabetes mellitus resembling the hypochloaemic form of diabetes insipidus.

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*STUDIES ON DISORDERS OF THE THYROID GLAND

III

FURTHER STUDIES ON THE PATHOLOGICAL AND CLINICAL SIGNIFICANCE OF DIFFUSE ADENOMATOSIS OF THE THYROID GLAND

EMIL GOETSCH, M D

BROOKLYN, N Y

In a previous paper read before this society at its annual meeting last year I (1) drew attention to an interesting group of border-line nervous patients who present many difficulties in diagnosis and treatment and who complain of symptoms resembling in many ways mild chronic hyperthyroidism, incipient tuberculosis, neuro-circulatory asthenia, effort syndrome, psychasthenia, psychoneurosis, neurasthenia and other allied nervous states. I reported the peculiar symptomatology of this group of patients and the diagnostic findings which led me to think we were dealing with a mild chronic hyperthyroidism. I furthermore reported a considerable success obtained after partial thyroid resection. The pathological findings in the thyroid glands were striking and led me to believe that we were dealing with a hitherto unnoticed type of thyroid pathology giving rise to a latent chronic hyperthyroidism, a condition which I called "Diffuse Adenomatosis." I wish to describe in some greater detail the symptoms and pathology of these cases and to point out what I consider the clinical and pathological significance of this group of thyroid disorders.

I may review briefly the history, symptomatology and differential diagnosis of this group of patients in the hope that similar cases may be properly diagnosed and that more may receive the benefits of what seems to be promising therapy for some of them. These patients are mostly women between the ages of twenty and thirty with the following symptoms—asthenia, fatigueability, loss of weight and strength, nervousness of varying degrees, labile pulse with mild tachycardia, tremor, perspiration, vasomotor instability, mental depression and worry and often a slight

* Read at the Fifth Annual Session of the Association for the Study of Internal Secretions, Boston, June 6, 1921

elevation of temperature It is not at all surprising that these patients suffer under a variety of diagnoses of which incipient tuberculosis, psychoneurosis and neurasthenia may be mentioned In fact several of my patients had been under medical care for years and in several instances had been sent to tuberculosis sanatoria under the impression that they were suffering with tuber-

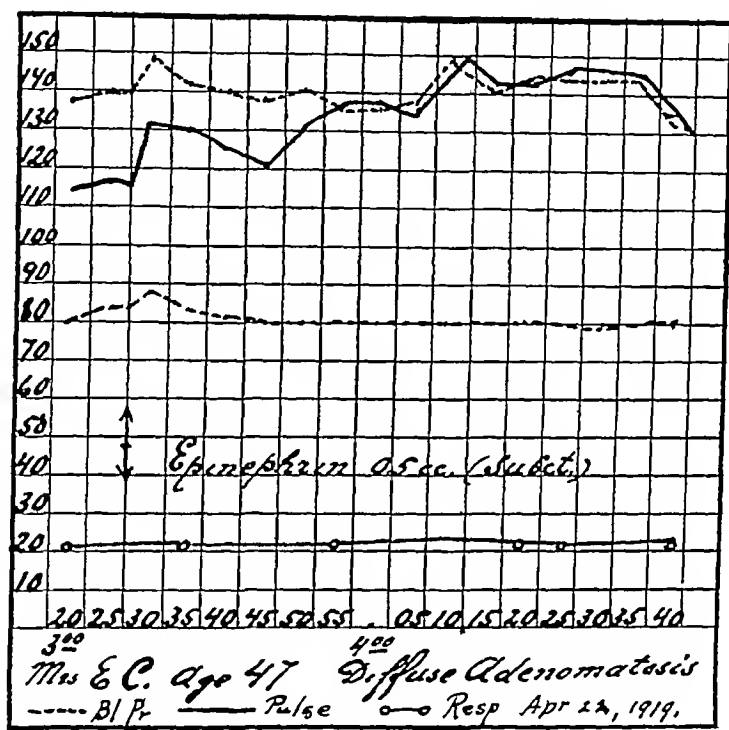


Fig 1 Graphic chart of a moderately positive epinephrin hypersensitiveness test in a case of "diffuse adenomatosis" the thyroid gland of which is shown in microscopic section in Figs 4 and 5 Note the early moderate rise of systolic pressure and the rather definite and sustained rise of pulse from 110 to the highest 144 reached about 40 minutes after the injection of 0.5 cc epinephrin chloride Very slight change in diastolic pressure No change in respirations

culosis, only to discover, after several months of rest régime, that there was little or no tuberculosis present Others had wandered from physician to physician in search of relief and were finally diagnosed as psychoneurotics

Speaking of clinical signs and findings, I may say that these patients do not present the well known cardinal signs of hyperthyroidism as we meet them in adenoma and in exophthalmic goitre There is nothing peculiar noted about the eyes, the signs we find in exophthalmic goitre are absent, the thyroid gland is often slightly or moderately enlarged, but may be neither visibly

TABLE I

Symptom chart of a positive epinephrin test obtained in the same patient whose chart is shown in Fig 1. Note the early and sustained rise of pulse and the moderate rise of systolic pressure and the expression of signs and symptoms produced by the injection, such as increased throbbing, feeling of faintness, marked tremor erythema, general trembling and vasomotor changes.

April 22, 1919 Pre operative Epinephrin Hypersensitivity Test.
(Goetsch) Mrs E G Age 47 Johns Hopkins Hospital Med No 41971

Clinical Diagnosis Moderate hyperthyroidism

Operation June 18, 1919 Double partial lobectomy of thyroid gland

Pathological diagnosis Diffuse adenomatosis

Time	Pulse	Resp	B P	Clinical observations
3 20	114	20	137/80	Slight nervousness Palms moist No tremor
3 25	116		140/84	of extended fingers Some throbbing over heart and back No flush of face
3 27½	Subcutaneous injection—Epinephrin 0.5 cc (1:1000 sol.)			
3 30	132		148/88	Marked subjective symptoms. Feels faint. Jump in throat Throbbing of abdominal aorta. Tremor in hands Trembling
3 35	130	20	148/88	Macular erythema of left side of face
3 40	126		140/82	Patient complains of burning of face Trembling
3 45	122		138/80	over entire body Diffuse erythema of face Nervousness increased
3 50	132		140/80	"Face does not burn now." Erythema fading
3 55	136	20	142/80	"Heart is beating harder."
4 00	136		140/80	
4 05	138		142/80	
4 10	148		148/80	
4 15	142		144/80	Symptoms gradually disappearing
4 20	144	20	138/80	
4 25	144	20	138/80	
4 35	144		136/80	Tremor in hands not so marked as a half hour ago
4 40	132		134/80	

Interpretation. A moderately positive hyperthyroid reaction as indicated subjectively by marked increase of symptoms and signs characteristic of hyperthyroidism and objectively by a sustained increase in pulse and systolic blood pressure.

nor palpably enlarged and, therefore, escapes notice as being the probable etiologic factor. When palpated the thyroid gland is fairly firm, elastic and does not show the presence of nodules as in adenoma, again thrills and bruits are absent. There may be a mild tachycardia, the pulse is labile but at rest may be normal. A fine tremor is usually present, and the hands are cold and clammy as a rule. The patient is underweight, looks run-down and asthenic and pallor is usually noted. Perspiration is also excessive.

The diagnosis of the true underlying condition in these patients is in part made by exclusion, in part by more direct evidence such as chronic symptomatology and a positive epinephrin test, to be mentioned again. The majority of my patients had had medical treatment over long periods of time, as much as several years in a few instances with little or no benefit. This alone

makes me suspicious, since incipient tuberculosis and also various nervous states so often yield to rest, diet and medicines. The complaint is characteristic of a mild chronic hyperthyroidism, though to be sure, not pathognomonic of it. Finally I am able to demonstrate a hypersensitiveness of these patients to my epinephrin test (Fig 1, Table 1), which gives such a typical response in hyperthyroidism. In pure tuberculosis my test is negative (fortunately for the differentiation of diffuse adenomatosis from incipient tuberculosis), and in the other allied conditions, such as effort syndrome, psychoneurosis and neurasthenia, the test is either distinctly atypical, does not give what I have described as a positive hyperthyroid response, or is entirely negative.

I should like to emphasize a few points in the history of these patients which help to differentiate the latter from cases of neuro-circulatory asthenia, psychoneurosis and neurasthenia. One often finds that in these conditions the complaint is variable and vague and dates far back into childhood. The onset of the trouble is very indefinite, in fact one is tempted to think that the condition is inherited, since it frequently begins in childhood, and one often finds that the parents are of nervous type. I am inclined to believe that we are dealing with a constitutionally inferior nervous system in some of the allied states. Hyperthyroidism or dysthyroidism (and under these I have grouped these cases of diffuse adenomatosis), usually has a definite starting point. The patient generally knows when her symptoms began and very often dates them from the time of puberty, whereas before that time she may have been in very good health and entirely well. The neurasthenic or psychoneurotic on the other hand often does not remember when she really felt well. The symptoms may begin after pregnancy and sometimes after an acute infection such as "flu" or pneumonia. Again, the complaints in hyperthyroidism are usually quite definite and characteristic, whereas in the allied functional nervous states the complaints are frequently varied and extremely vague.

Unfortunately, I am unable to report the metabolic rate determination in this series of patients, as most of them were observed previous to a year ago, at which time I was not determining metabolic rates as a routine in my thyroid patients.

However, after I first drew attention to this group of thyroid disorders, Woodbury (2) made a number of determinations upon this type of patient and found that the metabolic rate is not particularly increased, in fact it may be normal or only slightly abnormal. As I pointed out last year, I think Woodbury is correct in assuming that regardless of the normal metabolic rate these patients were suffering with hyperthyroidism. It would seem that the epinephrin test, which is more sensitive than the metabolic rate determinations, is positive in these individuals, though mildly so, and hence is in this group of more diagnostic value than the metabolic test. This finding is somewhat similar to that found in the quiescent phase of adenoma at which time the metabolic rate is found to be normal, whereas, since the hypersensitiveness of the sympathetic nervous system is a persistent characteristic, the epinephrin hypersensitiveness is even then positive.

Working on the assumption that these patients were suffering with some kind of chronic thyroid intoxication, on account of the characteristic symptomatology, the failure to gain after ordinary measures and the positive epinephrin test, I decided to resect the thyroid gland. Knowing that no harm would be done, I decided to operate with the full permission and understanding of both patient and physician. These patients were all too ready to undergo any measures at all, a fact which made it doubly necessary that operation should only be done as a last resort and after other measures had failed. Otherwise, I was well aware that needless operations would be done in patients not well chosen or properly diagnosed.

The thyroid gland is found to be slightly or not at all enlarged in "Diffuse Adenomatosis." It has the dark pink color of the hyperplastic gland. On palpation it is found to have a granular or lobulated feel, the consistency is slightly firmer than normal but definite nodules are not felt. The delivery of the thyroid lobe is sometimes difficult because of the periglandular adhesions which are frequently found. There is an increased vascularity, the cut surface tends to bleed rather profusely. There is a diminished amount of colloid in the gland, thus distinguishing it from the simple colloid goitre, and the consistency is not as firm as in exophthalmic goitre, nor is there the character-

istic lobulation seen in the latter. These changes are uniform throughout the entire gland.

Upon microscopic examination (Figs 2, 3, 4) we find the striking and characteristic change to be a marked increase of interstitial cells scattered diffusely and in large numbers throughout the gland with an associated atrophy and almost complete disappearance in some areas of the colloid acini. The interstitial cells are readily recognized as being epithelial and not connective tissue or lymphoid cells by the fact that they possess a considerable amount of protoplasm and have a fairly large, round, vesicular nucleus with abundant chromatin granules. The cells have no definite arrangement, are present in large numbers throughout the gland, and by pressure cause atrophy of the true alveolar epithelial cells. Here and there abortive attempts at the formation of young, small alveoli are recognized, and occasionally large, clear cells with large nuclei are seen filling the spaces in these acini which are ordinarily occupied by the colloid. The appearance is one of desquamated cells arising from the epithelial alveolar cells lining these new-formed acini. Then again here and there hyperactive looking acini with little colloid, tall columnar lining cells and large, dense nuclei are seen. These have the appearance of exophthalmic goitre acini. They are few but striking in appearance and so different from the appearance of the majority of the acini, which are often separated from one another by an apparent invasion of the interstitial tissue, and are smaller than those in the normal gland, also much less numerous, and lined by flat, atrophic looking alveolar cells. In a few instances, lymphoid cell accumulations are seen, but these are readily distinguishable from the interstitial cells by their small pyknotic nuclei and lack of protoplasm.

These findings are the precise opposite of those found in colloid goitre, puberty hyperplasia and exophthalmic goitre, in all of which there is a conspicuous absence of interstitial cells, conditions none of which could possibly be confused with diffuse adenomatosis. On the other hand, the opposite might also be expected and is in fact found in diffuse adenomatosis, for as we have seen there is a marked increase in the interstitial cells with an atrophy and even disappearance of the colloid acini. As I have previously pointed out, in cases of adenomata, tumors

which are toxic and arise from individual groups or nests of interstitial cells, there is an associated atrophy and regression to form the simple colloid picture in the thyroid gland outside of the adenoma. This result may be analogous to the production of an inactive colloid gland by the experimental administration

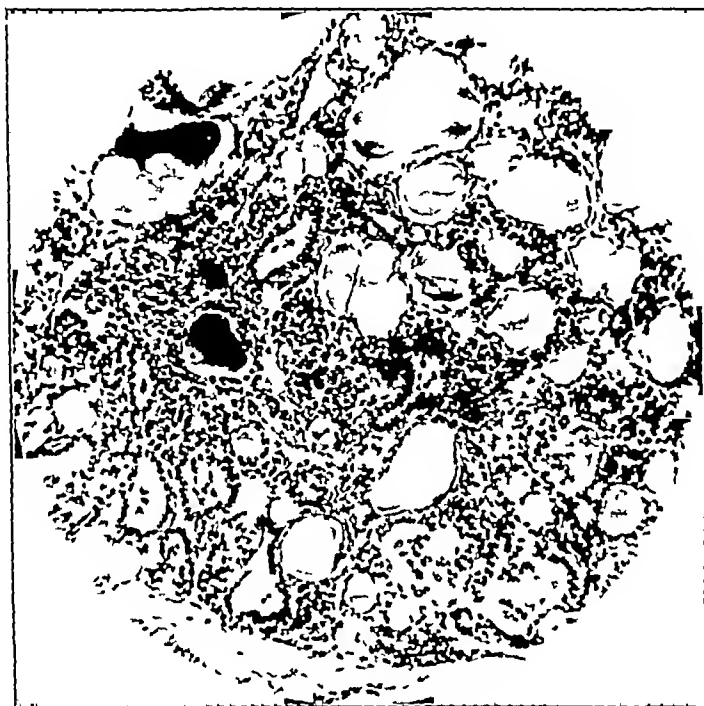


Fig. 2. Low power (Proj. oc. No. 2 Obj. 8 mm achromat. Camera length 28 in.) photomicrograph of section from thyroid gland of a woman of 47 years who had a chronic complaint lasting over several years consisting of palpitation of the heart with paroxysmal attacks of tachycardia, weakness, nervousness with tremor, depressions and indigestion. No relief under prolonged medical measures. Chief findings were: no exophthalmos, slight enlargement of the isthmus of the thyroid gland, lateral lobes not palpable. No nodules, no bruits felt. Slight fine tremor of the fingers. Palms moist. Feet cold. Hypotrichosis. Reflexes at the knees active. General clinical findings were: temperature 98 to 99.6. Pulse averages 70 when patient is calm and at rest but frequently runs up to 110 and 120 with excitation or under emotion. Moderately active epinephrin hypersensitivity test.

Operation June 18, 1919. Bilateral partial resection of the thyroid gland. Good post-operative recovery.

Note the abundance of interstitial cells separating the atrophic colloid acini. One sees in the midst of the interstitial tissue several new formed acini which are lined by tall columnar active looking epithelial cells in sharp contrast with the low flat atrophic acini of the remaining thyroid gland.

of iodine or iodides to animals, such as the opossum (Bensley) and the dog and sheep (Maine). In the case of the adenoma the toxic material or possibly hormone is furnished by the cells of the adenoma arising, as we believe, from the foetal cells of

DIFFUSE THYROID ADENOMATOSIS

Cohnheim, in the meantime there is no call for the secretion of the normal thyroid alveoli, which consequently atrophy and become inactive. The same atrophy and inactivity are found in the remaining colloid acini of the gland in diffuse adenomatosis, another indication by analogy that there is a hormone or toxic



Fig 3 Low power (Proj oc No 2 Obj 8 mm achromat Camera length 28 in) photomicrograph of section (5 mm thickness haematoxylin and eosin) from the thyroid gland of a young woman of 20 years who complained principally of nervousness, worry, crying spells, trembling dysmenorrhoea weakness and loss of memory. The chief findings were absence of eye signs slight uniform enlargement of the thyroid gland but without nodules or bruits. Slight tremor. Reflexes generally increased. Pre-operative epinephrin test definitely moderately positive.

Operation Nov 29 1915 by Dr E Goetsch. Partial resection of right thyroid lobe excision of isthmus and small portion of left lobe. Very good recovery and marked post operative improvement.

Note the great abundance of interstitial tissue the lymphoid cell accumulation below and to the right and the growth of cells in the indefinite acini in the midst of the interstitial tissue. Note also the relative absence of acini which are atrophic in appearance.

production of thyroid secretion on the part of the interstitial cells, otherwise why should the colloid acini atrophy? It is not pressure altogether, if at all for I have found this atrophic colloid change even in the normal opposite lobe in cases of unilateral

adenoma Another indication of the inactivity of the alveolar cells in both of these conditions is the almost complete absence of mitochondria (3) in the acinar epithelial cells We know hyperthyroidism can be produced by adenoma, the cells of which I believe have the same origin as the interstitial cells in diffuse adenomatosis Should we not expect, therefore, symptoms pro-

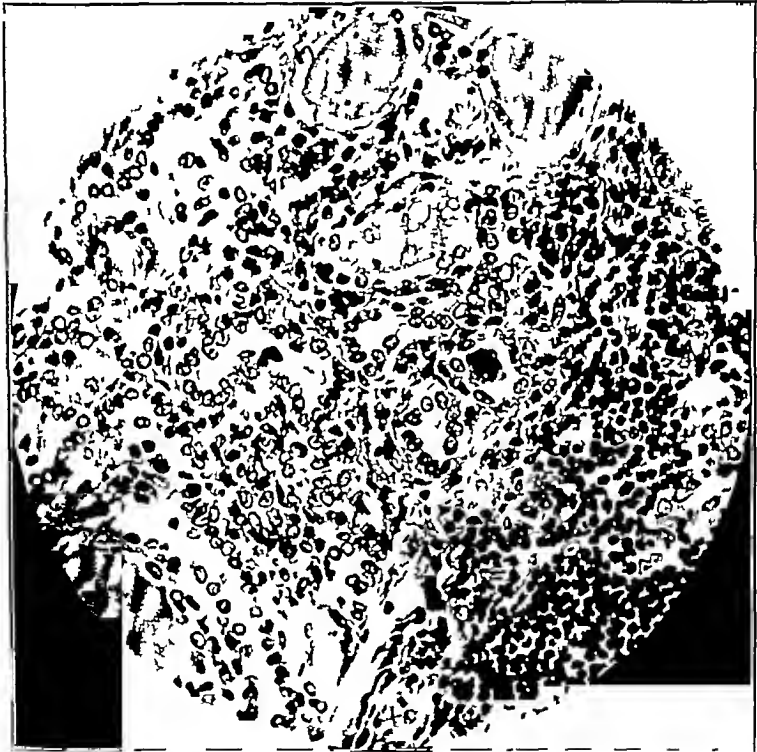


Fig 4 High power (Proj oc No 2 Obj 4 mm apochromat Camera length 28 in) photomicrograph of area within the dark circle in Fig 3 Note the distinct epithelial nature of the interstitial tissue in sharp contrast to the lymphoid cell accumulation shown in the right of the section Note the abortive irregular new formed acini lined by the large protoplasmic cells and enclosed within the interstitial tissue These newly formed acini appearing more active than the old atrophic acini of the original thyroid gland as shown at the upper and lower edges of the photograph

duced by the secretion of the interstitial cells similar to symptoms found in cases of adenoma? Such I believe to be the case As I had previously shown, the foetal adenoma (3, 4), before degeneration sets in, is histologically active in appearance, as indicated by the rich mitochondrial concentration in the cells A similar richness of mitochondria is often seen in the interstitial cells of

diffuse adenomatosis All these arguments are in favor of the view that we have in diffuse adenomatosis a toxic thyroid state, or a dysthyroidism depending for its symptomatology upon a marked hyperplasia and hyperactivity of the interstitial cells

There are many points of similarity in the symptomatology of adenoma and diffuse adenomatosis, and why should there not be, if, as I believe, the intoxication depends upon activity of thyroid epithelium derived in both instances from the interstitial cells The nervous and mental symptoms are much the same Emotionalism, depressions, melancholia, impaired memory, and even talk of suicide are common complaints The pulse is labile rather than accelerated, and vasomotor symptoms are frequently found together with increased perspiration Excision of the adenoma is commonly found to relieve these symptoms, and just so resection of the thyroid gland, which reduces the amount of interstitial tissue in diffuse adenomatosis, has rendered patients of the latter group very much improved To be sure, in diffuse adenomatosis, just as in exophthalmic goitre, one cannot remove all the offending thyroid tissue, hence the relief is not quite so striking in diffuse adenomatosis as in adenoma operation In both instances the epinephrin test is moderately positive, and according to Woodbury (2), who has examined a series of these cases, the metabolic rate is not increased in diffuse adenomatosis, nor in the quiescent phase of adenoma Pathological change, however, is always present and characteristically gives varied symptoms, according to the degree of activity at any one moment present I think one cannot deny that there is a dysthyroidism present simply because the metabolic rate is not distinctly increased, for when a normal metabolic rate is established in certain adenoma cases, relief of symptoms follows only after excision of the adenoma

I feel that we are dealing with a clinically very significant group of nervous people whose diagnosis and treatment in the past has been most obscure There is doubtless a very considerable percentage of patients in the so-called borderline group of nervous disorders who belong to the sub-group of thyroid gland disorders which I have termed "Diffuse Adenomatosis" I feel that more of these cases will be recognized if the trouble is taken to follow the advice I have given as to the importance of a very

careful history of the complaint, the establishment of a beginning point of the trouble, the failure of general measures and the positive epinephrin response. I want to state most emphatically that I do not feel that the majority of so-called borderline cases such as described, are thyroid cases and should be subjected to surgical measures. I do, however, feel that a percentage of these are thyroid disorders, which can be reasonably readily recognized after the measures advocated, and that in my experience a very considerable success has been obtained in a small series of cases after partial resection of approximately three-fourths of each thyroid lobe.

Turning now again to the pathology of this interesting condition, I may recapitulate to say that in the development of the early foetal thyroid gland two epithelial elements are recognized: first, the alveolar or parenchymal thyroid cells which form the colloid acini characteristic of the thyroid gland, and, second, the undifferentiated or perhaps dormant epithelial cell-nests, the so-called foetal or interstitial cells which are found in the interstices between the acini of the gland. In the normal gland the acini are fairly regular and there is a small amount of interstitial tissue. In the pathological evolution of the gland to form the various types of goitre with which we are familiar, we find that the alveolar epithelium may regress or atrophy, the colloid spaces distend, apparent partial disappearance of interstitial tissue takes place, and we have the simple colloid gland (Fig 5). In the more actively functioning conditions of the alveolar epithelium alone, leaving aside the interstitial cells, we find alveolar hypertrophy and hyperplasia, giving rise to hyperthyroidism in puberty hyperplasia, and finally also in exophthalmic goitre (Fig 5). Turning now to the interstitial cells, we find that individual islands of these cells may give rise to the discreet encapsulated foetal adenoma (Fig 5), which in turn gives rise to hyperthyroidism. If now the cellular stimulus, whatever it may be, affects uniformly and stimulates to overgrowth the interstitial cells everywhere in the gland, then we have finally the condition in which I have become greatly interested, namely, "Diffuse Adenomatosis" (Fig 5). The alveolar epithelium here undergoes atrophy and regression and the thyroid intoxication, I believe, is due to overaction of the abundant interstitial tissue.

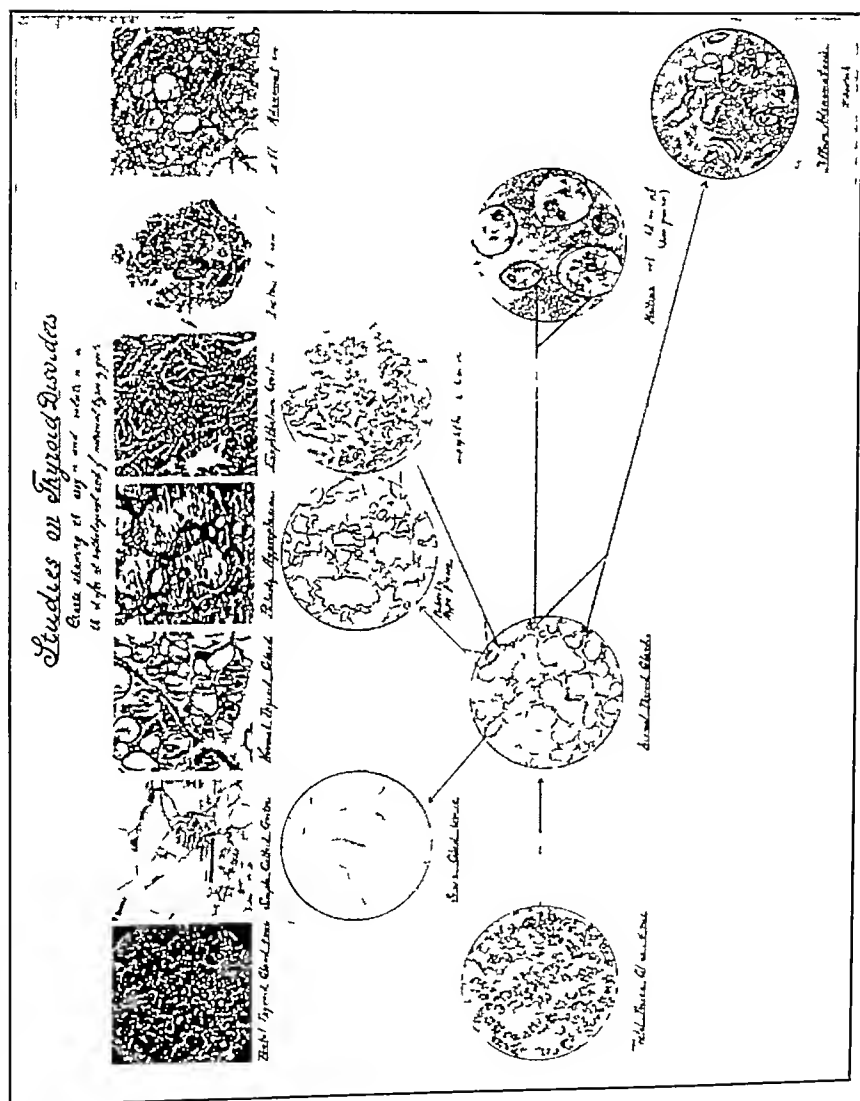


Fig. 5. Chart semidiagrammatic to show the derivation of the various pathological types of goitre from the two original epithelial elements in the thyroid gland the acinar or alveolar epithelium and the interstitial or foetal cells. In the order of their activity and origin from the alveolar epithelium we have, first the retrogressive relatively non-functioning simple colloid goitre then the various degrees of function and hyperplasia as represented by the normal gland, puberty hyperplasia and exophthalmic goitre. From the foetal or interstitial cells are derived the adenoma and finally I believe the diffuse adenomatosis, as I have described it. The chart illustrates the derivation and the pathological position and significance of Diffuse Adenomatosis in the various groups of goitre.

So far as I know, what I have just elaborated is a new conception in the pathology of goitre. I feel, therefore, that we are dealing with a new group of individuals suffering with thyroid disorder. It is a significant group, clinically, both from the point of view of symptoms and treatment. From a pathological standpoint, I feel after a study of diffuse adenomatosis that we are dealing with a new pathological division of goitre which on microscopic section is just as characteristic as are puberty hyperplasia, adenoma or exophthalmic goitre. Whether the toxin produced is of the exact nature of thyroxin or not, or whether it is the same as that produced by adenoma, are questions which cannot be answered at the present time. Whether the disease should be considered hyperthyroidism in the same sense as adenoma or perhaps dysthyroidism consequent upon an altered secretion, are questions similarly unanswerable at the present time. That the secretion elaborated might be of a different character from that in the normal gland or in exophthalmic goitre is possible since the symptomatology is similarly somewhat at variance with these conditions. It may be that the different character of the disease is due to the fact that we are dealing with a chronic mild hyperthyroidism extending over some years of time, a fact which might readily give rise to a different syndrome than is found in the more acutely toxic thyroid states.

Realizing these facts, I feel that "Diffuse Adenomatosis" will be more often recognized by physicians who become acquainted with the symptoms, signs and diagnosis, particularly the differential diagnosis of this condition, and in a considerable number of instances relief may be offered by referring these sufferers to the surgeon for partial thyroid resection. Finally I wish to emphasize the great care one must exercise in the diagnosis and treatment of these individuals in order not to be open to the serious criticism of performing futile thyroid operations upon nervous individuals wrongly diagnosed.

SUMMARY

Attention is drawn to that group of border-line nervous patients who present many difficulties in diagnosis and treatment and who complain of symptoms resembling, in many ways, mild chronic hyperthyroidism, incipient tuberculosis, neuro-

circulatory, asthenia, effort-syndrome, psychasthenia, psychoneurosis, neurasthenia and other allied nervous states. Some of these patients are suffering from a true thyroid disorder, perhaps dysthyroidism. There is no exophthalmos in diffuse adenomatosis. The thyroid gland is usually slightly enlarged, but does not present thrills and bruits. It shows a striking increase in the interstitial cellular tissue and atrophy, or partial disappearance of the colloid acini, a histological picture different from other forms of goiter. The patients react positively to the author's epinephrin hypersensitiveness test, whereas the metabolic rate may be within normal limits and therefore if the diagnosis of thyroid disorder were to be made purely upon increased metabolic rate, these patients would be overlooked. Treatment consists of resection of approximately three-fourths of each thyroid lobe. Considerable success has been attained in a small series of cases.

The term diffuse adenomatosis is restricted to the condition in which there is a general diffuse overgrowth of the interstitial epithelial cells as against the hyperplasia of the normal alveolar epithelium. The origin and nature of diffuse adenomatosis is a new conception in the pathology and clinical significance of thyroid disorders.

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ADRENAL FEEDING IN CONDITIONS OF HYPERTHYROIDISM*

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Certain derivatives of the entire adrenal gland produce physiological reactions which differ materially from those of commercial adrenalin (Parke, Davis & Co)

The materials tested have been the nucleoproteins, the globulins and the coagulable albumens obtainable from aqueous extracts of this organ, and the non-coagulable "residue" of this extract. The latter is prepared as follows. After the precipitation by acetic acid of the nucleoprotein material from an aqueous extract of the hashed fresh (beef) adrenal glands, the filtrate is made slightly alkaline with NaOH and boiled to remove the alkali albumens, this filtrate is then again acidified and boiled to remove the acid albumens. There then remains a final dark-colored filtrate representing a non-coagulable somewhat hydrolyzed aqueous extract of the gland which, for lack of a better name, has been designated as the "adrenal residue." This is very rich in a pressor substance closely similar to epinephrin, but produces much more vigorous and lasting reactions, especially upon the stomach and pancreas, than do corresponding doses of adrenalin chlorid. An alcohol extract of the entire gland acts very similarly to this residue but not quite as intensively.

While studying these adrenal derivatives in comparison with adrenalin, it was found that they were all vasoconstrictors, apparently in proportion to their epinephrin content, but differed decidedly from the latter material in that they all exhibited an inhibitory or "check" effect upon secretory activity, which was by no means in proportion to their epinephrin content. The results upon the pancreas, and particularly upon the stomach, were quite striking and seemed to indicate some clinical value in the adrenal nucleoprotein material which rather vigorously checks the total quantity of the gastric secretion and

* From the Johnston Livingston Fund for Experimental Therapeutics, Cornell University Medical College, New York City

also decreases its acidity and more or less inhibits gastric peristalsis. Corresponding doses of adrenalin showed few or none of these "check" effects, which seemed to be brought about by stimulation of the functions believed to be mediated by the terminal filaments of the sympathetic in contradistinction to those of the autonomic system. Incidentally, it was found that the hypodermatic administration of the adrenal residue or of an alcohol extract of the gland (made by evaporating the alcohol and adding water until the epinephrin content was equivalent to that of the residue) produced anorexia, vomiting and extreme prostration, and the frequent repetition of the dose was liable to cause death.

Because these derivatives of the gland showed such striking inhibition of the alimentary tract, it was decided to test their effects upon the iodine content of the thyroid, especially as our experiments seemed to indicate a marked degree of physiological antagonism between derivatives of the thyroid and those of the adrenal glands.

It has long been known that the thyroid gland in Graves' disease, or conditions of hyperthyroidism, contains less than the normal amount of about 0.5 mg. of iodine per gram of gland substance. Moreover, the severity of the disturbance seems more or less to correspond to the degree of the thyroid's iodine loss, or to the degree of its inability to hold iodine. Consequently, any medicament which experimentally makes the thyroid gain in iodine should be of some therapeutic value.

Dogs were employed in the tests, and it was first learned that the extirpation of one thyroid lobe resulted, in untreated, healthy animals, in a gain of some 20 per cent to 30 per cent of iodine in the remaining lobe. The maximum gain seemed to be reached at the end of three or four weeks. Intercurrent malnutrition, or disease like mange, apparently lessened this gain. At the time of the second operation no gross change in the size of the thyroid lobes could be detected. Only those animals were employed which seemed in vigorous condition, and in which both lobes on inspection, appeared to be alike. Under ether, one lobe was then removed, trimmed, weighed and its iodine content determined by the Kendall methods (1). In

the preliminary tests the Riggs method (2) was used, but was later discarded in favor of the Kendall method which gives more uniform and trustworthy results. The same individual made all of these numerous iodine tests.

After excising one thyroid lobe from each of twelve selected animals, they were all then fed on a standardized diet consisting of cracked meal, evaporated milk, casein, lard, and bone ash, which was previously ascertained to maintain the nutrition and metabolism at a constant level. With this diet there was mixed daily for the first group of three, 0.016 gm of adrenalin crystals (Parke, Davis & Co), for the second group, 2 c.c. of the adrenal residue (Schieffelin & Co), which contained an equal amount (0.016 gm) of epinephrin—like material calculated by Folin's method (3), for the third group, 4 gm of the adrenal nucleoprotein material (Schieffelin & Co). This latter was a rather arbitrary dosage, as the nucleoproteins contain only faint traces of epinephrin. The fourth group of three dogs received only the standard diet and were retained as "controls." At the end of forty-five days (or considerably later than the period at which the maximum gain in iodine had previously been ascertained to take place in the single remaining thyroid lobe) the second thyroid lobe was excised from all the animals, weighed and tested for iodine. There were noted some slight variations in a gain or loss of gross weight in these (second) excised lobes, but the changes could be traced to differences in the trimming of foreign tissue or to the variations in the amount of blood. These variations, however, seemed to bear no relation to the changes in the iodine content, which were quite marked.

The thyroids of the "control" animals gained the normal average amount of about 30 per cent in iodine. Those fed the pure (commercial) crystals of adrenalin showed a slight increase over this, but so little that it was judged to come within the limits of error. In short, the results of adrenalin feeding were negative. But the group which was fed the adrenal nucleoprotein material showed a considerable increase, or an average gain in iodine of about 50 per cent. Those fed the adrenal residue exhibited the greatest gain, or on an average of 70 per cent*.

* A detailed statement of these experiments has been accepted for publication in the *Am. J. Physiol.* for March 1922.

Although this series is rather too small to permit any very sweeping conclusions, the results agree so perfectly with many rather rough preliminary tests that there can be little doubt of some direct influence of the adrenal gland upon the thyroid. This influence seems to be exerted not so much by the active principle of the medulla or epinephrin, as by a combination of this with some other material, possibly from the cortex or from the entire organ, for the adrenal nucleoprotein material, with its mere trace of epinephrin, seemed to make the thyroid gain much more iodine than did a great deal larger dose of the adrenalin crystals. The latter, as previously stated, show a practically negligible effect. That this influence of the adrenal nucleoproteins, and especially of the adrenal residue, upon the thyroid is one of "check," or inhibition, seems very probable because, as mentioned previously, of what is known of the iodine content of the thyroid in health and in conditions of its excessive secretory activity or hyperthyroidism. The administration of iodine to these patients is generally contraindicated because of the well known danger of producing a violent exacerbation of the disease. Apparently, the hyperthyroid gland is unable properly to metabolize the iodine which usually reaches it, and when this amount is increased the epithelium seems to proliferate and break down and form little or no colloid material.

As yet, we can only speculate as to how this takes place. But the formulation of a theory is legitimate and a very necessary precedent to an exact knowledge of the process which seems to involve the involuntary nervous system and its functions.

The chief symptoms of *typical* hyperthyroidism, or conditions in which there is supposed to be a superabundance of the thyroid product, are referable to hyperactivity of the autonomic group of these nerves. Practically the only evidence of sympathetic involvement is the tachycardia, which is supposed to depend upon irritation or stimulation by the thyroid, of the cardio-accelerator or a sympathetic nerve. But the vaso-dilatation, the sweating and the signs of gastrointestinal activity are all evidences, not of sympathetic, but of parasympathetic or vagus, stimulation. Furthermore, in the typical cases, the tachycardia is something more than a mere increase in the rapidity of the heart action. There is a certain degree

of violence in the contractions which is very suggestive of vagus participation. Thus, clinically at least, the evidences of the disturbance in which the thyroid is believed to be abnormally active are all traceable to hyperactivity of the functions believed to be performed by the terminal filaments of the parasympathetic nerves.

Experimentally, the coagulable materials which can be isolated from the thyroid, when injected into animals, produce no appreciable immediate reaction. But the non-coagulable extracts, like one made with alcohol or a slightly hydrolyzed aqueous extract designated as the thyroid residue and prepared like the adrenal residue, are vigorous vasodilators and stimulants of the gastric and pancreatic secretions. These effects are produced apparently by direct stimulation of the terminal filaments of the parasympathetic or vagus group of nerves, which are believed in general to produce dilatation of blood vessels and increase in secretory activity (6). There are thus non-coagulable derivatives of the thyroid which excite immediate and definite physiological reactions.

Because these consist in stimulation of the functions believed to be performed by the parasympathetic or vagus portion of the involuntary nerves, and because this group shows marked activity in cases of typical hyperthyroidism, it is reasonable to believe that the thyroid product acts upon and through these particular nerve terminals and not through the sympathetic. Furthermore, because of the thyroid's well-known stimulating effect upon general metabolism, and because of the demonstrably stimulating effect of non-coagulable extracts of the thyroid upon some, if not all, parts of the parasympathetic system, the function of the product of the gland seems, broadly speaking, to be concerned with the production of energy in all the organs and tissues. In short, its function can be summarized as that of "drive."

Impulses which are antagonistic to those conveyed in the parasympathetic group of nerves seem to be discharged through the sympathetic terminals. Both are believed to be distributed to every organ, but to supply opposing impulses, or those which produce vasoconstriction and, in general, inhibition of functional activity. The action of the sympathetic nerves, with which the chromaffin tissue of the adrenal gland is so closely

associated, is thus apparently opposed to the thyroid-autonomic or vagus system, and can be summarized as that of "check"

As stated previously, derivatives of the entire adrenal gland like the nucleoprotein material, and especially the adrenal residue, apparently intensify this check of the nerve impulse much more vigorously than the epinephrin of the medulla. All of these derivatives contain more or less epinephrin. The latter, therefore, seems to be in the living animal only a stable component of a possibly larger and more labile product. However this may be, the stimulation or intensification of the check nerve impulse by these derivatives of the (entire) adrenal gland, like the stimulation of the drive by the thyroid, must be chemical. That is, the adrenal product after entering each cell must chemically restrain or "check" its metabolism, while the thyroid product on the other hand chemically accelerates or "drives" it. But each of these processes seems to depend upon the functional integrity of the nerve endings. For if these are lacking or are rendered functionless by poisons, as can be demonstrated in the stomach, the usual stimulation produced by the thyroid derivatives is absent. It is not as easy to destroy or paralyze the gastric sympathetic terminals and so demonstrate their importance for the action of the "check" derivatives of the adrenal. But these extracts have a stimulant effect upon the contraction of voluntary muscles, and this action is apparently exerted through the nerve end plate (5). The function of this organ can be completely abolished by fatigue and then the injection of the adrenal derivatives fails to excite a response. If, however, the fatigue is not complete, that is, if some response to electrical stimulation is still obtainable, the injection of the adrenal derivatives will immediately restore the vigor of the muscular contractions.

This fatigue experiment has considerable significance, not only in showing that the adrenal product probably acts through or upon the nerve terminals, but in suggesting the frequent origin of the hyperthyroid disturbance in a fatigue and consequent failure in functioning in the sympathetic or check mechanism. For if fatigue of the motor nerve end plate can abolish the influence of the adrenal product in voluntary muscles, fatigue of the involuntary or sympathetic nerve terminals in the viscera should interfere with or abolish their "check" influence. Be-

cause of the presence of epinephrin in all of these adrenal derivatives and its well known affinity for the sympathetic terminals, there is every probability that the normal adrenal product contains at least an epinephrin-like substance, and consequently acts through or upon the sympathetic endings and so intensifies or stimulates their apparent check function. Fatigue of the involuntary nerves, though it has not actually been demonstrated, undoubtedly follows the same laws which govern the fatigue and abolition of function in the voluntary nerve endings. If then fatigue should occur in the sympathetic terminals around the thyroid epithelium, the adrenal product could not act and the normal check upon the metabolic activity of the thyroid would fail. The result should be hyperthyroidism.

Clinically, these disturbances are so much relieved by rest and so much intensified by fatigue, that fatigue of the sympathetic or check portion of the involuntary nervous system seems to be the primary and most frequent cause of these functional thyroid disturbances. They also seem to follow infections, and hence there is every probability of the occurrence of a toxic damage or destruction of the restraining sympathetic terminals. Then total loss of function would cause the adrenal product or adrenal feeding to be useless. If only partial, the adrenal product or adrenal feeding would be more or less effective, as suggested by the partial loss of function by fatigue in the experiments with voluntary muscle. If the loss of function is not complete, the injection of the adrenal derivatives, as stated previously, restores the full vigor of muscular contractions.

To recapitulate this theory for hyperthyroidism and the influence upon the iodine content of the thyroid by feeding the adrenal nucleoproteins or the adrenal residue. The thyroid epithelium is supposed to receive a parasympathetic (vagus) nerve supply which accelerates or "drives" its metabolism of iodine, and a sympathetic which "checks" it. The product of the thyroid containing iodine, after its utilization (or any ingested thyroid material or ingested iodine), returns to its epithelial source, where it enters the epithelium only through the intermediation of the parasympathetic nerve terminals. The ensuing chemical processes, or metabolism into a normal thyroid product, requires the normal functionation of the sympathetic or "check" nerve terminals in the thyroid through which the

is high and especially when there are signs of excessive gastrointestinal activity, the nucleoprotein material with its low epinephrin content seems to be more valuable than the adrenal residue. The adrenal residue, with its high epinephrin content, on the other hand, seems valuable in the average case in which the blood pressure is low and the gastrointestinal activity not excessive. Although the thyroid product with its contained iodine is supposed to return to its source and not be destroyed or excreted, there ought theoretically to be some advantages in combining with the adrenal feeding the administration at the same time of small doses of iodine. Practically, it will often be noted that neither medicament alone will be as efficient as both together, but when taking iodine in any form, a patient with hyperthyroidism should always be warned that if the gland swells or "feels tight" the iodine should be stopped. If this gross change in the adrenal product alone can exert its restraint. If either the sympathetic terminals or the adrenal product fail, the thyroid's metabolism of iodine becomes defective or too rapid and hyperthyroidism is the result.

Of course, the most obvious criticism of this theory is that hyperthyroidism does not follow Addison's disease, but in this condition the sympathetic nerves are presumably intact and the adrenal product cannot be assumed to be the only material which affects the tropic functions of the sympathetic. Experimentally, the fact remains that feeding derivatives of the entire adrenal gland to dogs causes the animal's thyroid to gain noticeably in its iodine content. Why the feeding of one adrenal derivative should be more effective in causing the thyroid to gain in iodine than the feeding of another, is a matter for speculation. But, clinically, in cases of hyperthyroidism, when the blood pressure gland is neglected there is grave danger of an ensuing acute and often dangerous exacerbation of the hyperthyroidism. Very little iodine seems generally to be required. Three to five drops of the official tincture in a half glass of water once or twice a day is usually sufficient and may be too much.

The following case histories are illustrative.

CASE I G W, age 20, broker's clerk, after a prolonged period of hard work with late hours, was first observed in January, 1917, with typical exophthalmic goiter of three or four months' duration. There were marked exophthalmos, considerable, pulsating, symmetrically

enlarged goiter, pulse rate, 120 to 130, blood pressure, 120, weight, 145 lbs

On Feb 2, 1917, under local anaesthesia, both inferior thyroid vessels were tied, and on Feb 9th, both superior vessels and a portion of the upper ends of both lobes were at the same time excised

In April, the evidences of hyperthyroidism, with the exception of the goiter and some exophthalmos, had practically disappeared. The pulse rate was 80, and the weight 165 lbs. In June, work was resumed, and later all the symptoms gradually returned

Nov 13, 1918. Under ether, two-thirds of each lobe was excised and all the vessels in sight were, of course, tied and cut. There was a somewhat stormy convalescence, and the patient left the hospital at the end of a month improved, but still with marked signs of hyperthyroidism

Jan 9, 1919, there was moderate exophthalmos, the goiter, just after operation imperceptible, was now noticeable, the pulse rate was 100 to 110, blood pressure, 160, weight, 134 lbs. Weakness and diarrhoea were the chief complaints. Two 1-grain tablets containing 10 per cent of the adrenal nucleoproteins were then given every two hours. This form of adrenal feeding apparently had an immediately beneficial effect upon the diarrhoea, and the patient began to gain weight, which gradually increased during January and February to 150 pounds. The blood pressure fell from 165 to 145, but the pulse rate continued from 110 to 120

In March, 1919, the adrenal residue in 10-drop doses every two hours was substituted for the adrenal nucleoproteins, and during the next month the pulse rate decreased to an average, while quiet, of about 90. But there was still noticeable exophthalmos and a goiter which, in spite of the liberal excision in the second operation, was as large as at the beginning of the disease. Then iodine, in the form of 1-grain pills of iodide of iron, was given three times daily. Within a few days the general condition appeared practically normal, but the goiter was perceptibly larger and firmer. The iodide of iron was, therefore, ordered to be discontinued. Two weeks later this patient was found with a rather violent exacerbation of his hyperthyroidism, apparently due to the iodine, which had been continued in spite of directions to the contrary. There was a temperature of 102, the pulse rate was 150 to 160, the blood pressure, 160, and the sweating and diarrhoea had returned

During the next two weeks with feeding the adrenal nucleoprotein tablets, which seem particularly beneficial for the cases with diarrhoea, the symptoms gradually improved. When the gastrointestinal disturbance had subsided, feeding with the adrenal residue was resumed in 10 or 12 drop doses every two hours

On May 15th, the pulse rate was about 90, but irritable, the blood pressure, 140, and the exophthalmos and goiter, noticeable. The 1-grain iodide of iron pills were then given one daily, but at the end

of ten days, although the hyperthyroid signs had nearly disappeared, the goiter began to swell and was accompanied by a feeling of pressure in the neck. The iodine was, therefore, immediately stopped until the uncomfortable cervical sensation had disappeared, and the goiter felt soft. By a little cautious experimenting, it was finally found, after another two weeks of the feeding with the adrenal residue, that the 1-grain iodide of iron pill could be taken every second day with apparent great advantage and without any subsequent swelling and "tightening" of the goiter.

If the adrenal feeding were omitted for two or three days the goiter immediately began to enlarge and feel uncomfortable. Apparently, the iodide had to be accompanied with the adrenal feeding to insure progress, and during June it was found that the iodide could be taken daily. In July and August the combination of iodine and adrenal feeding gradually seemed to complete the cure of all the symptoms except the exophthalmos and the goiter. The latter, however, had entirely disappeared in October, and the following month there was no exophthalmos and the medication was omitted. In January, 1920, the weight had reached 170, and no abnormality other than the cervical scars could be detected. This patient has continued well.

CASE II Mrs. A. M., age 42, presented a typical case of rather severe exophthalmic goiter, with slight exophthalmos, and only a just perceptible and symmetrical, firm enlargement of the thyroid. There was some pigmentation of the skin, considerable emaciation, much nervous irritability and frequent bowel movements. The weight was 86 lbs., pulse rate was 110 to 120, and the systolic blood pressure was 215. This patient had been confined to bed with a general sedative treatment for several weeks. Jan. 18, 1916, two 1-grain tablets containing 10 per cent of the adrenal nucleoproteins were given every two hours with an almost immediate relief of the frequent bowel movements and a more gradual decrease in the tachycardia.

On Feb. 15, the pulse rate averaged about 90, the weight had increased to 92 pounds, and the systolic blood pressure had fallen to 150. The goiter was softer, but the exophthalmos, unchanged. Operation was declined, as the improvement seemed to promise a recovery.

In September, 1916, after a period of considerable comfort and apparently following a few weeks of strenuous work, there was an exacerbation of the hyperthyroidism which was accompanied by a systolic blood pressure of 210. Feeding for about three weeks with the adrenal nucleoprotein material again seemed to reduce this to between 140 and 150, and also all the other symptoms. At the same time, the weight increased. One-grain iodide of iron pills were then added, one daily, to the adrenal feeding, and at the end of the month practically all of the symptoms had disappeared. This patient, later, again relapsed and again improved, and operation under the circumstances seems to offer little hope of a permanent cure.

CASE III F N, age 38, a salesman, presented typical exophthalmic goiter of several weeks duration March 10, 1921, moderate exophthalmos, considerable symmetrical goiter, circumference of neck $15\frac{1}{2}$ inches, weight, 150 lbs, pulse rate, 120, blood pressure (systolic), 160, were noted He was given the 1-grain pills of iodid of iron, three daily, and warned to stop them if they caused swelling of the neck or any cervical discomfort At the end of two days both the swelling and discomfort were noted, and, after discontinuation of the iodine, these signs soon disappeared

March 22, 1921, the adrenal residue in 10-drop doses every two hours was then administered, with rapid improvement, especially in the subjective nervous irritability The pulse rate was 90, blood pressure (systolic), 150, weight, 152 pounds There was a slight decrease in the exophthalmos and goiter

April 15, 1921, the patient returned after a month's rest in Atlantic City The pulse rate ranged from 80 to 90, blood pressure was 145, weight, 155 pounds One-grain iodid of iron pills once daily were now added to the adrenal residue, with warning as to the repetition of its possible ill effects

May 23, 1921, gain much more than before taking the iodine was noted The pulse rate was 82, blood pressure, 132, weight, 163 pounds The circumference of the neck was $14\frac{3}{4}$ inches, showing marked decrease in goiter, the exophthalmos was less pronounced The patient returned to work.

Sept. 12, 1921, the medication of the preceding month was discontinued and again marked and typical symptoms developed, but there was no loss of weight Operation was advised, but at present the patient is again trying rest and the combination of iodid of iron with the adrenal residue

SUMMARY

Experimentally, the feeding by mouth to dogs of derivatives of the entire adrenal gland, especially the adrenal nucleoproteins and a slightly hydrolyzed aqueous extract known as the adrenal residue, causes the animal's thyroid to gain from 50 to 75 per cent or more in its iodine content within a few weeks

Feeding with corresponding amounts of adrenalin crystals is without appreciable effect upon the thyroid

In conditions of hyperthyroidism the thyroid gland contains less than the normal amount of iodine per gram of gland substance

The failure thus indicated of the thyroid to retain its normal amount of iodine apparently is due to a defect in the metabolism of iodine by the thyroid epithelium, and this defect is the probable biochemical cause of the disturbance

The defect in the thyroid epithelial metabolism is theoretically dependent upon some preceding defect in the chromaffin, or automatic "check" system, and primarily begins in a failure in functioning of the thyroid terminals of the sympathetic nerves. It seems probable that the adrenal product acts through or upon these nerve terminals and, therefore, the functional integrity of these terminals is essential for the success of adrenal feeding.

Feeding with adrenalin, or the so-called active principle of the medullary portion of the adrenal gland, has no appreciable effect upon the iodine content of the dog's thyroid, and in human hyperthyroidism does not relieve the symptoms and may often intensify them (Goetsch test).

Three illustrative cases are cited.

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ADRENAL ENLARGEMENT IN RABBITS *

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It has been observed on numerous occasions that the feeding of thyroid extract to animals causes an enlargement of the suprarenal glands, but hitherto no attempts to determine the mechanism of this action have been reported. The present study deals with the effect of various factors on the enlargement of the adrenals, and affords some evidence as to the mechanism of enlargement after feeding thyroid extract. We have also acquired evidence to show that enlargements of the adrenals following thyroid feeding, major emotions, and trauma, involve the cortex much more than the medulla of the gland, if, indeed, the latter is involved at all.

The first careful study of the relation between the adrenal and thyroid was that of Rudinger, Falta and Eppinger (1), who concluded that thyroid feeding stimulated the adrenals, similar results were reported by Kostlivy (2). Schafer (3) states that "It may be assumed that the secretion of the thyroid in exophthalmic goiter acts as a direct stimulant to the suprarenal capsules, causing them to yield adrenalin to the blood in larger quantity, a result which is also obtained by thyroid feeding."

After intravenous injections of thyroid extract, Ott and Scott (4) found an increase in the adrenalin content of the blood in experimental animals, but they were also able to obtain a similar result by injecting other organ extracts. Gley and Quinquaud (5) carried out similar experiments from which they concluded that intravenous injections of relatively large doses of extracts of thyroid and other glands (pancreas and liver) increased the epinephrin content of the blood. However, it has been pointed out by Stewart and Rogoff (6) that such extracts lower the blood pressure. Consequently, the rate of blood flow through the gland is diminished with resulting concentration of epinephrin in the adrenal vein. Iscovesco (7) found hypertrophy of the heart, thyroid, adrenals, kidneys, testes, ovaries and uterus after injections of thyroid extract.

R. G. Hoskins (8) fed guinea pigs desiccated thyroid gland substance from birth and found that the adrenals of eighteen animals so fed weighed 0.059 gm. as contrasted with 0.047 gm. in eighteen control

* We wish to express our thanks to Dr. L. H. Newburgh for his suggestions and help during this work.

animals of equal age and weight. Later E. R. Hoskins (9) studied the relation between thyroid feeding and the growth of various organs in albino rats and found a distinct increase in the relative size of the adrenals of all thyroid-fed groups. He found the reaction relatively more marked in males, in which sex the gland is normally lighter.

Hering (10) fed rats fresh minced ox thyroid mixed with bread in milk and found that both the cortex and medulla participated in the general adrenal enlargement which resulted, but that the enlargement of the cortex was relatively somewhat greater.

Kuriyama (11) fed rats a dog-biscuit-lard-thyroid mixture in quantities containing 10 gm. of thyroid per day for four days and found that the epinephrin content of the adrenals remained constant. The determinations were made by the Folin method.

Stewart and Rogoff (12) have concluded that the entire liberation of epinephrin is controlled by the sympathetic, as section of this nerve above the diaphragm abolished the spontaneous secretion, whereas section of the splanchnic alone did not entirely prevent the liberation of epinephrin. With this in view, we were careful in the experiments recorded below to destroy the adrenal innervation completely. Cannon (13) has shown that many factors cause a secretion of epinephrin, especially the major emotions, pain, and asphyxia, and that removal of the adrenal glands abolishes the effects obtained from such stimulation. Our experiments show that in rabbits, at least, the endocrine mechanism is distinctly labile and that extensive experimental procedures would be sufficient if continued to cause an enlargement of the adrenals in this animal.

METHODS AND RESULTS

Rabbits exclusively were used in this work. At the beginning of each experiment the animal was weighed and a serial number tattooed on the ear. This is a very convenient and rapid method of marking animals and, so far as we know, has not been described. India ink is used. A clean pen is dipped in the ink and the number written on the ear by a series of dots just piercing the skin. We have found this method to leave numbers legible for months.

A few animals died from intercurrent infections or other causes as noted in the protocols, but the majority were killed by a blow on the head. Immediately after death the final weight was recorded. In every case the adrenals were removed at once carefully dissected free of fat, weighed on an analytical balance, bisected, the cortex measured, and the glands preserved in formalin. For histologic study specimens were embedded in paraffin and stained with haematoxyline and eosin. The necropsy was completed by examination of other organs in the gross and weighing the heart and kidneys. The former was washed free from clots before weighing.

A control group of fourteen rabbits received the same general care and was kept under conditions approximately the same

as were the experimental groups. The average weight of the animals in this group was 1732 gm. The average adrenal weight was 294 mg or 169 mg per kilo and the average width of the adrenal cortex was found to be 1.8 mm (Table 1).

Desiccated gland substance* was fed to a group of 15 rabbits. The thyroid preparation was mixed with sugar of milk, and put up in gelatin capsules. Each day one capsule was forced well down the throat by a short piece of small, soft rubber tubing. The thyroid dosage and the complete protocols are condensed in Table 2. The average weight of the animals of this group at the beginning of the experiment was 1812 grams and the average weight at the end was 1324 grams. The average weight of the adrenals was 444 mg or 245 mg per kilo of the original weight. Compared with the control series it will be seen that the adrenals of this group showed a definite increase in weight averaging 76 mg per kilo, an enlargement of 45 per cent over the normal. Neither the heart nor kidneys showed comparable enlargement, although the hearts of the thyroid fed series were slightly heavier than those of the control group, averaging 2.7 gm per kilo, as compared with 2.5 gm per kilo in the control series. The average weight per kilo of the kidneys of the thyroid fed series was 6.2 gm, that of the control group, 6.6 gm per kilo.

The adrenal cortices of the thyroid fed series measured 2.3 mm, an increase of 0.5 mm or 21 per cent over the normal controls. It is evident, therefore, that a great part at least of the increased adrenal weight can be attributed to cortical enlargement.

During the thyroid feeding a progressive enlargement of the adrenals was evident. The adrenals of four rabbits (Nos. 1, 3, 4, and 6), which received thyroid for less than 30 days, averaged 364 mg or 244 mg per kilo, those of three rabbits (Nos. 15, 11, and 14), which received thyroid for from 30 to 50 days, averaged 401 mg or 262 mg per kilo, those of three rabbits (Nos. 8, 19, and 17), which received thyroid for from 50 to 80 days, averaged 471 mg or 260 mg per kilo, and those of four rabbits (Nos. 10, 16, 12, and 13), which received thyroid for from 80 to 100 days, averaged 518 mg or 273 mg per kilo. For some reason (possibly a primary endocrine disturbance) rabbit

* The thyroid used was prepared and furnished by Parke Davis & Co. for experimental work.

TABLE 1 NORMAL CONTROL SERIES

No	Sex	Best Weight Gm	Final Weight Gm	Heart Weight Gm	Kidney Weight Gm	Adrenal Weight Mgm	Adrenal Weight per Kilo Best Weight Mgm	Adrenal Cortex Width Mm	Mode of Death
N	—	1720	1720	—	—	315	183	1 8	Killed by blow
C	—	1506	1506	—	—	227	150	1 5	Bled from carotid
5	—	1324	1324	3 5	7 0	222	167	—	Killed by blow
24	♂	1531	1040	3 7	12 9	230	150	1 3	Died—Cause?
A25	—	1520	1270	4 2	11 0	215	169	—	Died—Pneumonia
29	♂	1993	1993	4 2	10 2	350	175	1 8	Died—Peritonitis
40	—	2053	2053	5 4	11 6	340	165	1 8	Bled from carotid
42	—	2071	2071	4 9	12 7	400	193	—	Bled from carotid
43	—	1230	1230	3 5	10 0	195	158	1 8	Killed by blow
17	—	1438	1438	4 5	13 0	275	191	1 8	Died—Pneumonia
55	♀	2083	2083	6 3	15 4	470	225	—	Bled from carotid
56	♀	2064	2064	4 6	13 5	342	165	2 0	Bled from carotid
57	♂	1849	1849	3 6	12 0	225	121	2 0	Bled from carotid
58	♀	1870	1870	3 5	10 7	310	165	2 3	Bled from carotid
Average		1732	1686	4 3	11 6	294	169	1 8	

TABLE 2 THYROID FED SERIES

No	Sex	Best Weight Gm	Final Weight Gm	Heart Weight Gm	Kidney Weight Gm	Adrenal Weight Mgm	Adrenal Wt per Kilo Best Weight Mgm	Adrenal Cortex Width Mm	Total Thyroid Fed Mgm	Days Fed	Mode of Death
1	—	1570	1277	5 0	10 0	205	130	1 5	14	6	Killed by blow
3	—	1400	1187	4 8	15 0	427	305	2 0	20	26	Died—Cause?
4	—	1490	1150	4 0	—	485	325	2 8	20	28	Killed by blow
6	—	1550	1400	4 3	8 0	339	216	1 8	21	30	Killed by blow
8	—	2087	1183	4 0	9 7	355	170	—	85	61	Died—Cause?
10	♀	2762	9611	7 0	18 5	665	240	2 3	164	81	Killed by blow
11	—	1545	970	5 0	8 8	335	217	1 5	75	54	Dead—Caseous pneumonia
12	♀	1930	1022	5 0	13 5	455	235	2 0	205	91	Died—Pneumonia
13	♀	2090	1560	6 4	13 5	445	212	2 5	205	91	Killed by blow
14	—	2032	1170	5 4	14 3	600	295	2 7	77	55	Died—Cause?
15	—	1545	836	3 9	8 1	272	176	1 8	53	38	Died—Lay on side Heart occasionally irregular Emaciated
16	♀	1875	1691	5 0	14 5	760	405	3 5	165	81	Killed by blow
17	♀	1690	944	5 0	10 0	485	286	2 2	148	79	Died—Cause? Very thin Hair falling out
18	♂	1885	1678	5 7	12 5	265	140	2 0	165	81	Killed by blow
19	♂	1729	1186	5 0	12 8	575	332	3 5	143	78	Very weak Killed by blow Liver congested Heart flabby
Aver		1812	1324	5 0	12 0	444	245	2 3	104	58	

No 18 failed utterly to respond and both its absolute and relative adrenal weights were distinctly less than the averages for the control series. Consequently, it was not included in the last group. This progressive increase in adrenal weight is graphically represented in Fig 1.

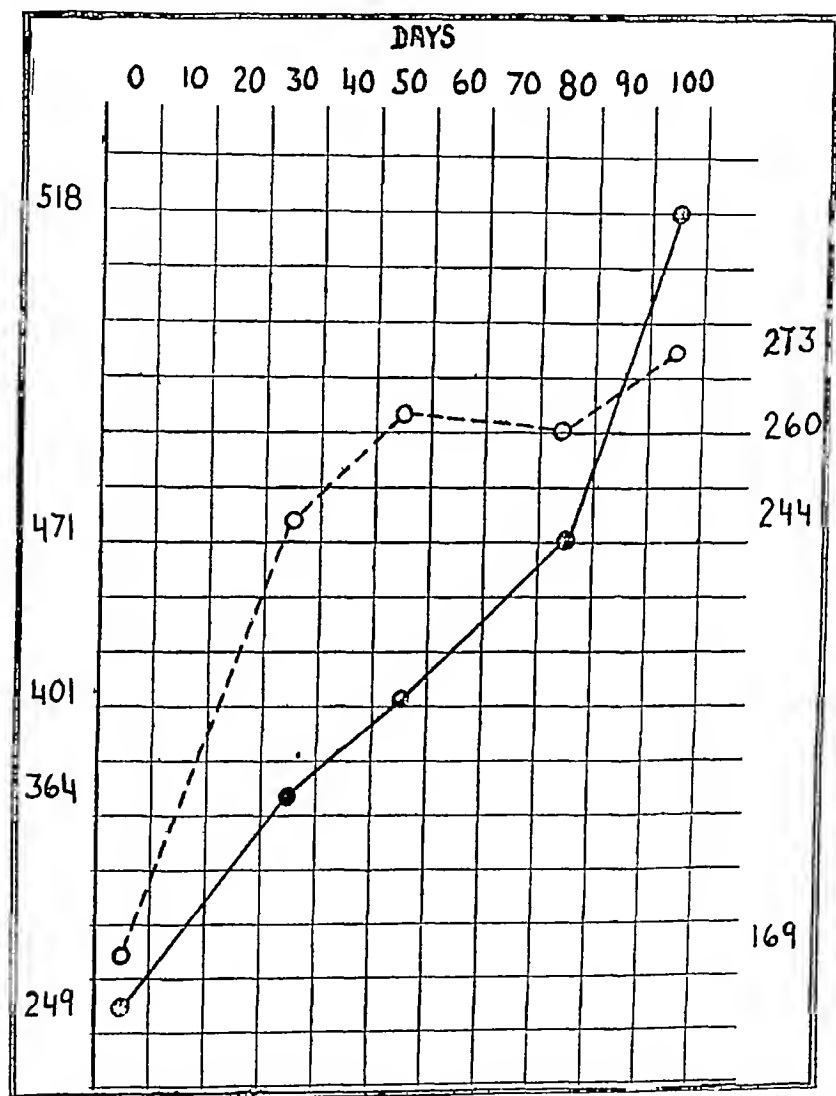


Fig 1. Progressive increase in adrenal weight during thyroid feeding of rabbits. Heavy line and figures at left represent absolute adrenal weights; dotted line and figures at right represent adrenal weight per kilo.

None of the adrenals of the thyroid fed series showed any striking histologic changes.

In order to determine what effect, if any, the splanchnic nerves had in the production of adrenal enlargement, two groups

of animals were studied. In each group the splanchnic innervations of both adrenals was sectioned with aseptic precautions under ether anaesthesia.*

The operation was performed through an incision in the anterior abdominal wall. The nerves were cut as close to the diaphragm as possible and in each case at least 0.5 cm. of nerve was destroyed. The difficulties of this operation in rabbits are not great on the left side, on the right, however, the gland and nerve lie posterior and in intimate relation to the vena cava and hepatic ligaments. In every case care was taken to dissect the connective tissue immediately surrounding the glands in order to be certain that every path of communication was cut. The gland itself was handled as little as possible and in no case was obvious injury done to it. The skin and fascia of the anterior abdominal wall were sutured with chromic catgut, usually in two layers. At necropsy no uncut fibrils of nerve were ever found. After the skin wounds had healed (generally in about ten days) one group of splanchnectomized animals was fed desiccated thyroid extract by forcing thyroid filled gelatin capsules down the throats with a soft rubber tube as already described. A control group of animals similarly operated upon received the same general care and was kept under conditions approximately the same as the thyroid fed group.

In the splanchnectomized control group the average weight of the animals was 1914 gm. at the beginning and 1544 gm. at the end of the experiment. The adrenals of the group averaged 482 mg. or 245 mg. per kilo of initial weight. It is to be noted that compared with the normal control series these adrenals averaged 76 mg. per kilo or 45 per cent heavier, an increase identical with that which was found after thyroid feeding. It is of interest also that the heart weight in the splanchnectomized control group was 2.7 gm., and the kidney weight was 6.2 gm. per kilo, corresponding exactly with the weight per kilo of these organs in the thyroid fed series (Table 3).

Thyroid feeding in the second splanchnectomized group of seven rabbits was continued for periods varying from 7 to 66 days. In this group the average weight of the animals at the beginning was 2722 gm. and at the end it was 1856 gm. The

* We wish to express our thanks to Nina A. Squier for assistance in anesthetizing the animals.

TABLE 3 SPLANCHNECTOMIZED CONTROL SERIES

No	Sex	Best Weight Gm	Final Weight Gm	Heart Weight Gm	Kidney Weight Gm	Adrenal Weight Mgm	Adrenal Weight per Kilo Best Weight Mgm	Adrenal Cortex Width Mm	Days After Operation	Mode of Death
64	♂	1966	1528	4 0	8 0	540	274	1 8	27	Killed by blow
60	♀	1600	1513	4 0	10 0	290	187	2 0	44	Killed by blow
63	♂	1932	1932	5 7	14 0	315	163	1 8	42	Killed by blow
86	♀	1925	1034	5 7	12 0	385	200	—	33	Dead—Cause?
89	♀	1620	1330	6 0	12 0	270	166	2 0	37	Killed by blow
93	♂	2240	2100	5 9	14 7	765	341	3 0	47	Killed by blow
95	♂	2120	1370	5 5	13 2	815	384	—	23	Dead—Cause?
Average		1914	1514	5 2	11 9	482	245	2 1	36	

TABLE 4 SPLANCHNECTOMIZED THYROID-FED SERIES

No	Sex	Best Weight Gm	Final Weight Gm	Heart Weight Gm	Kidney Weight Gm	Adrenal Weight Mgm	Adrenal Wt per Kilo Best Weight Mgm	Adrenal Cortex Width Mm	Total Thyroid Fed Mgm	Days Fed	Days After Oper- ation	Mode of Death
28	♂	2674	1495	6 2	12 7	705	263	3 2	35	7	28	Died—Cause?
31	♂	2703	1839	5 5	15 5	835	308	3 6	80	17	38	Died—Pneumonia
36	♂	3583	1974	9 0	14 9	680	189	—	185	42	75	Killed by blow
33	♂	2746	2030	7 5	12 3	995	362	3 0	675	66	88	Killed by blow
71	♂	3317	2265	8 2	16 5	865	260	3 9	200	20	32	Killed by blow
73	♂	2450	2080	7 5	12 0	690	281	—	1599	65	75	Killed by blow
84	♀	1580	1316	—	—	245	165	2 0	460	27	37	Died—Cause?
Aver		2722	1856	7 3	13 9	716	261	3 1	762	35	53	

average adrenal weight was 716 mg or 261 mg per kilo. The hearts of this group averaged 2.6 gm per kilo, and the kidneys averaged 5.1 gm per kilo. The adrenal cortices averaged 2.8 mm in width (Table 4).

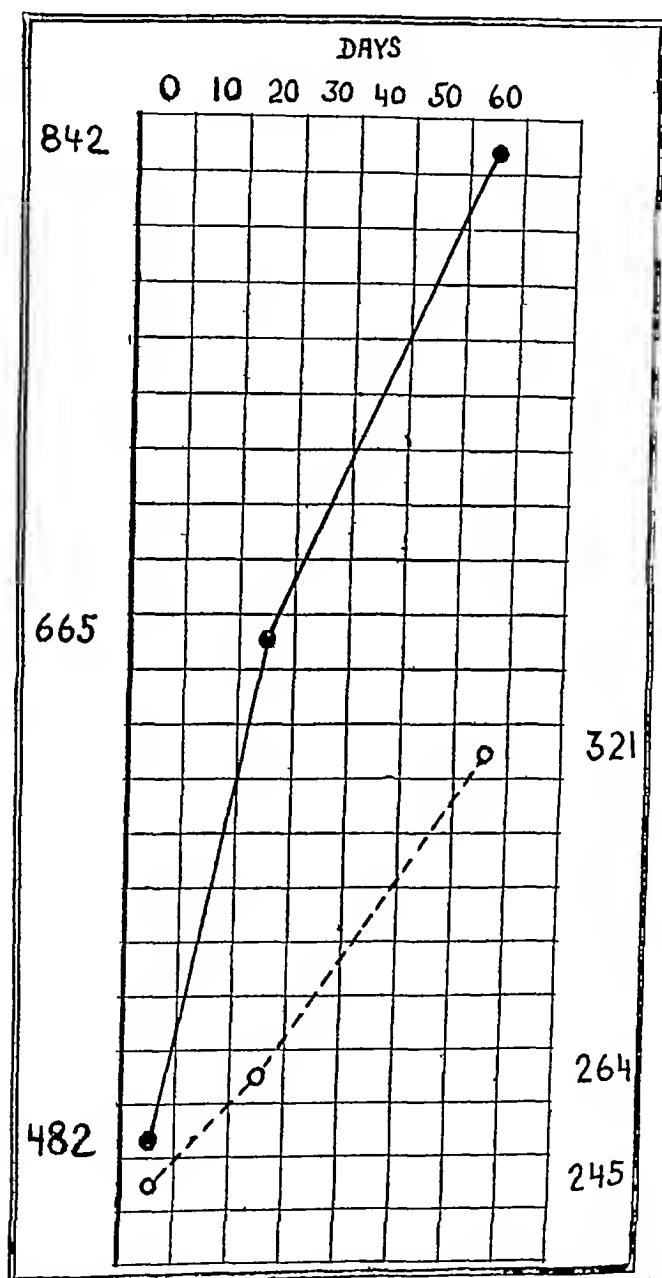


Fig. 2 Progressive increase in adrenal weight during thyroid feeding of rabbits in which the splanchnic innervation of the adrenals had been sectioned. Heavy line and figures at left represent absolute adrenal weights, dotted line and figures at right represent adrenal weight per kilo.

The same progressive increase in adrenal size during the period of thyroid feeding was noted in this group as in the un-operated thyroid fed rabbits. The adrenals of rabbits Nos 28,

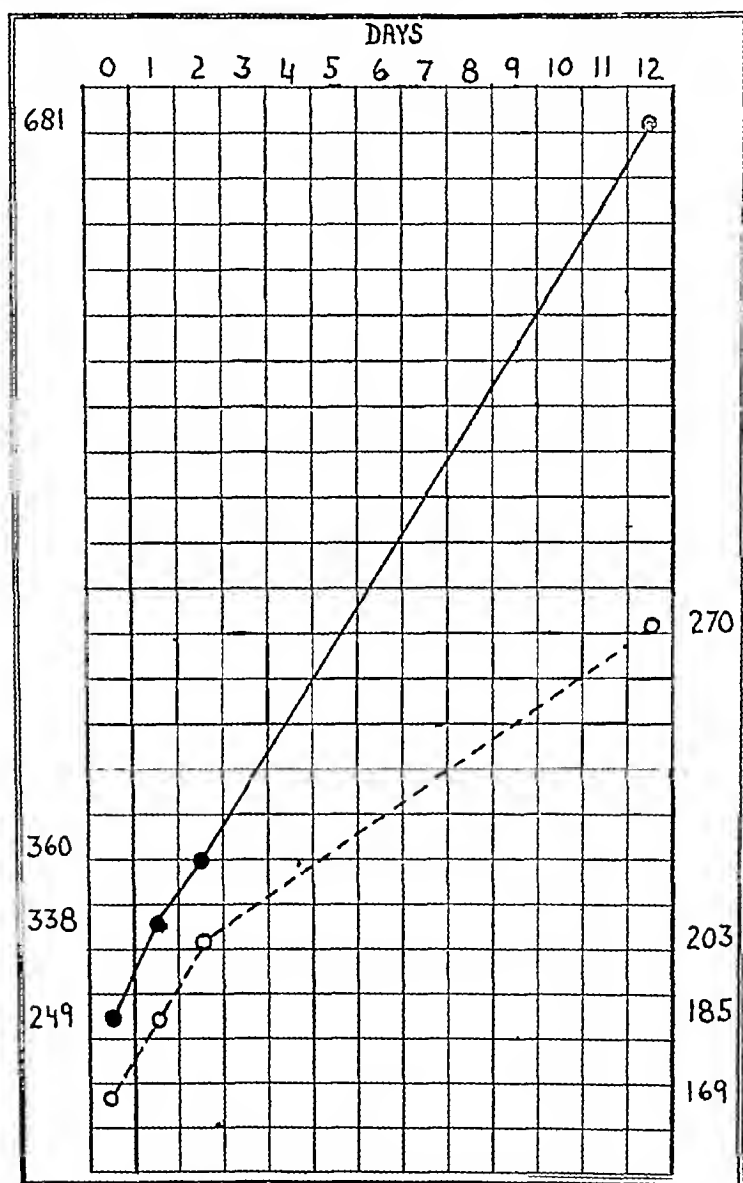


Fig 8 Progressive increase in adrenal weight resulting from continued trauma or shock. Heavy line and figures at left represent absolute adrenal weights, dotted line and figures at right represent adrenal weight per kilo

31, 71, and 84, fed thyroid from 7 to 27 days, averaged 665 mg or 264 mg per kilo, adrenals from rabbits 33 to 73, fed thyroid

TABLE 5 TRAUMATIZED SERIES

No	Sex	Weight Gm	Heart Weight Gm	Kidney Weight Gm	Adrenal Weight Mgm	Adrenal Weight per Kilo of Body Wt Mgm	Adrenal Cortex Width Mm	Mode of Death
20	♂	1776	—	—	310	174	2 0	Operated upon—Died on table
21	♂	1908	—	—	235	123	—	Operated upon—Died on table
22	♀	1385	—	—	330	238	2 7	Operated upon—Died on table
23	♂	1385	—	12 5	525	378	2 3	Fight—Died 10 days later
26	♂	1765	4 2	8 5	360	203	—	Operated upon—Died 2 days later
34	♂	2746	6 3	14 3	780	284	2 9	Fight—Died 12 days later
35	♂	3383	7 4	15 5	740	218	1 8	Operated upon—Died 12 days later
38	♂	2340	6 0	11 2	480	205	2 1	Operated upon—Died on table
		2086	5 9	10 3	470	228	2 3	

TABLE 6 SERIES TUBED WITHOUT THYROID

No	Sex	Original Weight Gm	Final Weight Gm	Heart Weight Gm	Kidney Weight Gm	Adrenal Weight Mgm	Adrenal Weight per Kilo of Original Weight Mgm	Days Tubed	Mode of Death
96	♀	2330	2190	5 0	10 4	1065	457	30	Killed by blow
97	♀	2295	2335	5 9	12 5	460	197	30	Killed by blow
98	♂	2135	2125	3 8	11 1	300	140	30	Killed by blow
99	♀	2155	2340	7 4	12 6	590	252	30	Killed by blow
100	♀	2145	2030	5 0	10 4	515	240	30	Killed by blow
		2212	2204	5 7	11 4	586	257	30	

65 days, averaged 842 mg or 321 mg per kilo (Fig 2) No important histologic changes were found in the glands of either of the groups of splachnectomized animals These results would indicate that, subsequent to the trauma and shock of operation, there is a definite adrenal enlargement quite comparable to that following administration of thyroid extract by the method described Furthermore, when thyroid extract is fed to such traumatized rabbits there is still greater increase in the size of the adrenals in spite of the fact that the nerve supply to the glands has been sectioned

It appeared evident from the results obtained in the splachnectomized control group that simple trauma and shock were sufficient to produce definite adrenal enlargement Consequently, it seemed advisable to study a group of animals from this standpoint alone Four animals (Nos 20, 21, 22 and 38) died on the operating table while splachnectomy was being done and the adrenals of these averaged 338 mg or 185 mg per kilo, very slightly heavier than the average weight per kilo of the normal adrenal series One animal (No 26) died two days after operation and its adrenals were found to weigh 360 mg or 203 mg per kilo No 35 died 12 days after operation, Nos 23 and 34 died about ten days after fights in which they were severely injured The adrenals of the last three rabbits averaged 681 mg or 270 mg per kilo (Table 5) Again in this series a progressive enlargement of adrenals was noted The longer trauma had been acting, the larger were the adrenals found to be A graphic representation of this result will be found in Figure 3 The severity of the trauma unquestionably would also be a factor, but in the cases cited the trauma in each case was approximately of the same intensity—sufficiently great to result in death

Since shock is sufficient to produce adrenal enlargement and since the adrenal enlargement of the untraumatized thyroid fed rabbits was no greater than in the splachnectomized control group, the question naturally arose whether simple intubation with empty capsules would not cause as much enlargement as was produced by the feeding of small quantities of thyroid Consequently, five rabbits were selected averaging 2212 grams in weight and for thirty days an empty gelatin capsule was daily forced down the throat of each with a soft rubber tube exactly as was done with the thyroid fed rabbits At the end

of the period the animals were killed by a blow on the head. The average adrenal weight of this group was 586 mg or 257 mg per kilo. Consequently, intubation alone is sufficient to cause a definite adrenal enlargement. Comparing the adrenal weights of this group with the average adrenal weights of rabbits Nos. 3, 4, 6, and 15, which were fed thyroid for 30 days, it will be seen that the adrenals of the thyroid fed animals averaged 282 mg per kilo or 25 mg per kilo heavier than the adrenals of the tubed controls. It is evident, therefore, that trauma or stimulation will produce an adrenal enlargement of apparently the same kind as that resulting from thyroid feeding, but that the same trauma or stimulation plus thyroid will produce still greater enlargement (Table 6).

DISCUSSION

The results of this work seem to point definitely to a thyroid-adrenal relationship. Cannon and Cattell (14) have shown that epinephrin causes an action current in the thyroid and that a similar result can be produced by stimulation of the splanchnic nerve. Other workers, as has been already mentioned, have found adrenal enlargement when thyroid gland substance was fed in a more natural manner, and our results show that the adrenal enlargement from thyroid capsule intubation is greater than that from simple intubation over a corresponding period of time. It seems very probable that any trauma or nervous stimulation of sufficient intensity results in increased secretion of thyroid hormone which in turn produces enlargement of the adrenal cortex. An increased width of adrenal cortex in experimental hyperthyroidism has been previously noted (15). We have shown that this enlargement does not take place as a result of stimuli passing along the splanchnic innervation of the adrenal glands for the enlargement occurs just as readily in animals in which these nerves have been cut. Consequently, it seems probable to us that the thyroid hormone acts directly upon the adrenal cortex.

Herring (16) did thyroidectomies on rabbits and found in a control group in which the thyroid gland was merely exposed that the adrenals averaged 200 mg per kilo, while in a similar group in which thyroidectomy was actually performed the adrenals averaged 172 mg per kilo. This last weight is practically the normal weight (169 mg per kilo). Viewed in the light of our

studies this effect is exactly what would be expected. In Heiring's control group the adrenal cortex was stimulated by the thyroid hormone liberated as a result of trauma, while in the thyroidectomized group the adrenals were of normal size because there was no thyroid available. In both groups he found the adrenals to have practically the same epinephrin content.

Many attempts to demonstrate thyroid-adrenal interrelation have been made through quantitative determination of epinephrin, but the majority of these investigations have omitted the adrenal cortex from consideration. The results have been conflicting and in general negative. On the other hand, our evidence as well as that of other workers seems to point conclusively to a definite relationship between the thyroid hormone and the adrenal cortex.

SUMMARY

1 The adrenals of rabbits fed desiccated thyroid extract by the method of intubation described averaged 245 mg per kilo, as compared with 169 mg per kilo in control rabbits. The enlargement was greatest in those animals fed thyroid over the longest period.

2 The adrenals of rabbits which had recovered from an operation in which splanchnic nerve supply to these glands had been sectioned averaged 482 mg or 245 mg per kilo.

3 The adrenals of rabbits which had recovered from an operation in which the splanchnic nerve supply to these glands had been sectioned and which were then fed desiccated thyroid gland by the method of intubation described averaged 716 mg or 261 mg per kilo. The enlargement was relatively greater in the adrenals of animals which had received thyroid over the longest period.

4 The adrenals of rabbits which had received traumatization sufficient to result in death averaged 470 mg or 228 mg per kilo. The enlargement was relatively greater in the adrenals of animals which had been subjected to trauma over the longest period.

5 The adrenals of rabbits mildly traumatized or stimulated by the intubation method used in feeding thyroid averaged 586 mg or 257 mg per kilo. The adrenals of rabbits receiving thyroid for a corresponding interval of time averaged 282 mg

per kilo or 25 mg per kilo more than the mildly traumatized group

6 The enlargement in all cases was largely if not entirely cortical

7 The enlargement was not accompanied by definite histologic changes

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THE EFFECT OF IODINE AND IODOTHYRINE ON THE
LARVAE OF SALAMANDERS I THE EFFECT
OF IODOTHYRINE AND IODINE ON THE
METAMORPHOSIS OF AMBYSTOMA
MACULATUM

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(From the Laboratories of the Rockefeller Institute for Medical
Research)

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In 1918 I made some preliminary experiments on the effect of iodine upon the metamorphosis of salamander larvae, these were entirely unsuccessful and the intention of making further experiments on this problem was given up. Soon after this, however, Swingle (1) published his first experiments on the acceleration, by inorganic iodine, of the metamorphosis of tadpoles and the correctness of my own observations became doubtful. Therefore, I have repeated, following closely the method employed by Swingle, my former experiments on the larvae of salamanders. These experiments confirmed in every respect the observations made during my first experiments and revealed the astonishing fact that exactly the same treatment, i. e., the administration of inorganic iodine, which produces precocious metamorphosis in tadpoles, has not the slightest effect on the metamorphosis of salamander larvae, although iodothyrene causes prompt metamorphosis in the salamander larvae just as it does in tadpoles.

THE INFLUENCE OF IODOTHYRINE AND IODINE ON THE LARVAE OF
AMBYSTOMA MACULATUM

In order to test the influence of inorganic iodine on the metamorphosis of the salamander larvae, two experiments, Experiments I and II, were carried out. The concentration of iodine used in these experiments was selected in accordance with the effect which iodine produced in similar experiments on the tadpoles of *Rana sylvatica*. With regard to the behavior of the salamander larvae kept in iodine solutions, as described below,

it may be pointed out that in these tadpole experiments a concentration of only 3 drops of a 1/20 M solution per 1000 cc of water was sufficient to cause a marked acceleration of limb development, while concentrations higher than 3 drops had a distinctly toxic effect on the tadpoles

Experiment I The eggs of one female of *A. maculatum* were freed from the common mass of jelly and placed into iodine-free water (10,000 cc H_2O , 0.16 gm Na_2CO_3 , 0.04 gm K_2CO_3 , 0.4 gm $MgSO_4 \cdot 7H_2O$ and 0.6 gm $CaCl_2$) This kind of water was used throughout the experiment The temperature was room temperature (about 25°C in average)

The larvae hatched on April 23, 1920, and on the same day were isolated into individual jars The experiment consisted of 3 series, a control series LXXXIV (containing 5 larvae, one of which was preserved for histological examination 40 days after hatching), an iodine series LXXXVIII (containing 6 larvae), and an iodothyrene series LXXXIX (containing 6 larvae) Earthworms were used for food

At an age of 14 days many larvae contracted an infection which resulted in a temporary retardation of growth (see Fig 1), but did not interfere with the experiment, as it passed off soon The growth as well as the course of the entire experiment are illustrated in Figure 1

20 days after hatching Nearly all larvae have developed 4 toes in the fore limbs and many have commenced to develop the first 2 toes in the hind limbs At this stage the larvae of the iodine series are placed into water containing 3 drops of a 1/20 M solution (in 95% alcohol) of iodine per 1000 cc of water (equivalent to 0.6 mgm iodine per 1000 cc water), the larvae of the iodothyrene series into water containing 0.1 gm iodothyrene (Bayer's powdered) per 1000 cc of water (equivalent to only 0.03 mgm iodine per 1000 cc water)

33 days after hatching At this date, 13 days after the first administration of iodothyrene, every single larvae of the iodothyrene series metamorphosed, although the size of the larvae was only 20 mm (see Table I)

34 days after hatching Since the iodine has not the slightest effect on the metamorphosis of the larvae, the concentration is increased to 5 drops of iodine per 1000 cc of water (equivalent to 1.0 mgm iodine per 1000 cc of water)

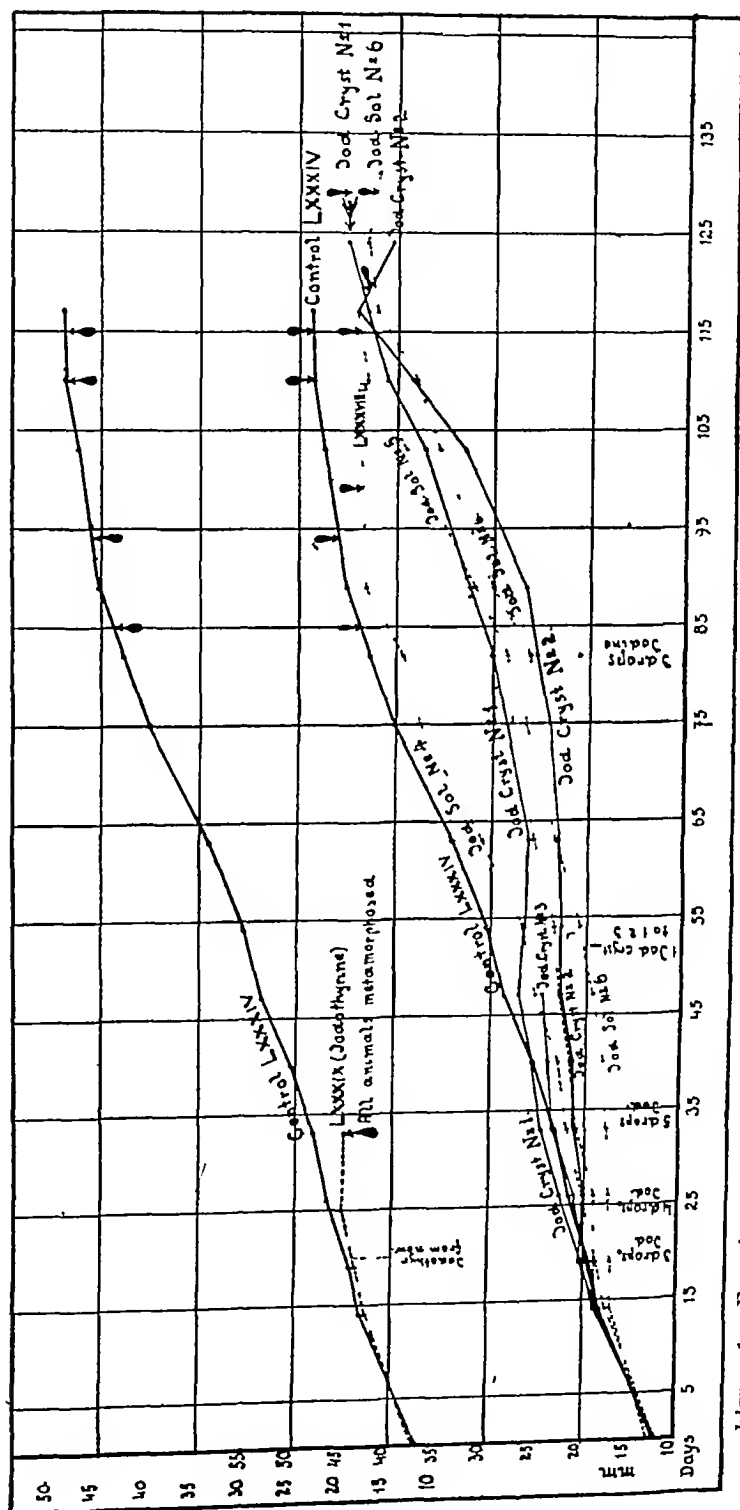


Figure 1 Experiment 1. The effect of iodine and lodothyryne on the metamorphosis of the larvae of *Ambystoma maculatum*. The thick black line in the upper and lower graph represents the growth of the control series LXXXIV (kept in iodine-free water). The dotted line of the upper graph represents the lodothyryne series LXXXIX. The three thin black lines and the three dotted lines of the lower graph represent each one individual of the iodine series LXXXVII, the three thin black lines illustrating the growth of the three larvae that were kept in the iodine solution and at the same fed iodine crystals, the three dotted lines representing the growth of the three larvae which did not receive crystals but were kept in the iodine solution. The amounts of iodine administered to the larvae are indicated on the bottom of the graph metamorphosis of every individual larva is indicated by an arrow.

52 days after hatching Since the iodine, except for a slight lowering of the rate of growth, had no effect as yet, it was suspected that the skin of the salamander larvae might be impermeable to iodine and that the small amounts of iodine swallowed with the water during feeding might not be sufficient to cause metamorphosis. Therefore, the larvae Nos 1, 2 and 3 of the iodine series were fed each one crystal of iodine. This resulted in an immediate check of growth (see thin black lines in Fig 1 at 54 days) and one larva (No 3), which had received the largest crystal, was found dead the next morning.

Aside from this toxic effect no particular action of the iodine was noticeable, no acceleration of metamorphosis was caused. In fact, the larvae of the iodine series metamorphosed at a later date than the controls (see Table I and Figure 1, in Fig 1 metamorphosis of each individual is indicated by an arrow).

In short, in the iodine series, metamorphosis, as is the case under normal conditions, was merely a function of growth, the larvae can not metamorphose before they have reached a certain size. That the size of the larvae of the iodine series was slightly

TABLE I

Experiment I Duration of larval period and size of the larvae at the time of metamorphosis

	Duration of larval period days	Size attained at the time of metamorphosis mm
Control	101	48.7
Iodine (solution)	122	45.2
Iodine (solution-crystals)	124	43.3
Iodothyrene	33	20.0

smaller, at the time of metamorphosis, than the size of the controls, was due to the poor feeding of these larvae, starvation alone, without the administration of iodine, always results in a slight decrease of the size at which metamorphosis takes place, combined with an increased duration of the larval period. In the iodothyrene series, however, metamorphosis is distinctly independent of growth, the larvae are considerably smaller (more than 58 per cent) at the time of metamorphosis and at the same time the larval period is greatly abbreviated (by 67 per cent).

Experiment II Quite similar was the result in another experiment. All larvae employed were from one female and were kept under the same conditions as those of Experiment I, in particular, iodine-free water was used in all series. In addition to earthworms, *Enchytraeus* and *Tubifex* were used as food. No infection occurred in this experiment.

The entire experiment consisted of 3 series, a control series LXXV (containing 6 larvae, one of which was killed for histological purposes before metamorphosis), an iodine series LXXIX (containing 6 larvae, 2 of which were killed for histological examination before metamorphosis), and an iodothyrene series LXXX (containing 6 larvae). The growth and metamorphosis as well as the entire course of the experiment are illustrated in Table II and Figure 2.

The iodine had no accelerating effect on metamorphosis, although in the beginning only a low concentration of iodine (2 to 3 drops of a 1/20 M solution per 1000 cc of water) was used so as not to interfere with growth. As this concentration, however, did not cause metamorphosis, the concentration of iodine was increased to 7 drops at an age of 60 days and to 8 drops of iodine per 1000 cc of water at an age of 63 days. Yet even this high concentration of iodine did not result in precocious metamorphosis. Again 3 larvae (Nos 1, 2, and 3, represented in Fig 2 by the thin black lines of the lower graph), were fed iodine crystals, the feeding being repeated several times and even two crystals at the same time being fed once to Nos 1 and 3. No 3 died from this overdose, the other two larvae did not show precocious metamorphosis. No 1 was killed for histological examination at an age of 82 days (3 of the control larvae had metamorphosed several days before this date), it showed no indication of metamorphosis. No 2 metamorphosed later than any of the control larvae.

TABLE II

Experiment II Duration of the larval period and size of the larvae at the time of metamorphosis

	Duration of larval period days	Size attained at the time of metamorphosis mm
Controls	80	52.2
Iodine (solution)	79	49.6
Iodine (solution-crystals)	89	40.9
Iodothyrene	58	29.8

The iodothyrimine series of this experiment received a dose 10 times smaller than that used in Experiment I, only 0.01 gm of iodothyrimine was added to each 1000 cc of water. Bayer's iodothyrimine, the preparation used in these experiments, contains 0.3 mgm iodine per 1 gm of substance. Consequently, the iodothyrimine larvae of this experiment received a dose of only 0.003 mgm iodine per 1000 cc water. Since the larvae of the iodine series were kept in a concentration of from 0.6 to 1.4 mgm of iodine per 1000 cc of water, the difference in the dose of iodine between the iodothyrimine and iodine series was still greater in this experiment than in the previous experiment. Yet, as Figure 2 and Table II show, metamorphosis of the larvae of the iodothyrimine series was again greatly accelerated and occurred precociously in regard to the size of the larvae as well as to the duration of the larval period. The size of the larvae, at the time of metamorphosis, was 43 per cent less than that of the controls, and the larval period was shortened by 28 per cent.

To summarize the results of Experiments I and II it seems evident that in salamanders metamorphosis cannot be accelerated by inorganic iodine, although iodothyrimine (even if administered in doses containing much smaller amounts of iodine than those employed in the iodine experiments) promptly results in metamorphosis.

It may be mentioned that two experiments were carried out in which the embryos of *A. maculatum* were subjected to the influence of iodine and iodothyrimine. In these experiments, too, iodine had no influence, while iodothyrimine caused metamorphosis at a very early larval stage. Since these experiments will be described in detail elsewhere, I may confine myself to the above brief mention.

DISCUSSION

While in the larvae of the Salientia the administration of inorganic iodine causes precocious metamorphosis (2), the same procedure is incapable of accelerating the metamorphosis of the larvae of the tailed amphibians. That the ineffectiveness of inorganic iodine is not due to the employment of too low a concentration is shown by the fact that in both experiments the concentration of the iodine in solution was much higher than the concentration of iodine in an effective dose of iodothyrimine, and the larvae fed crystals of inorganic iodine, in both experi-

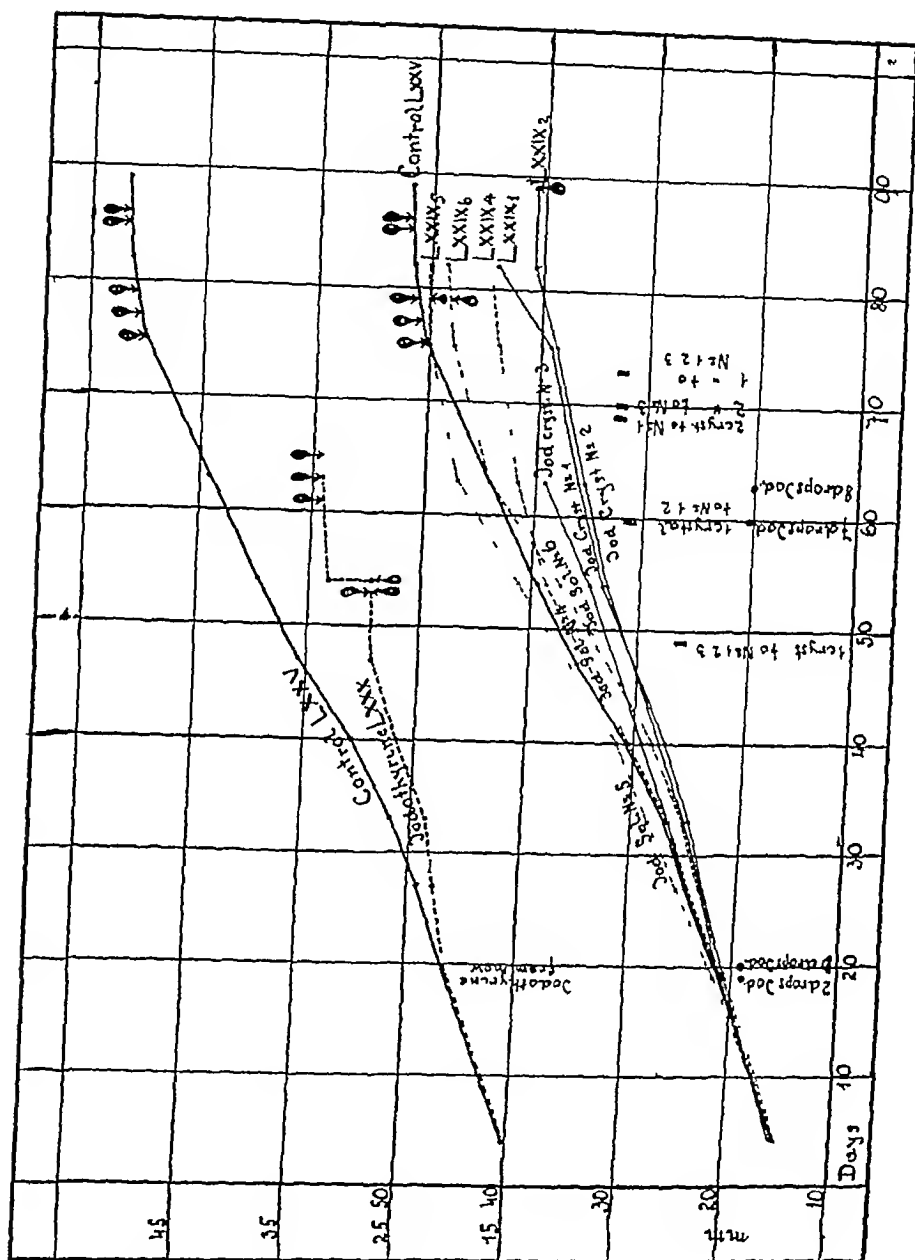


Figure 2 Experiment II The effect of Iodine and Iodothyrine on the metamorphosis of the larvae of *Ambystoma maculatum*. The thick black line in the upper and lower graph represents the growth of the control series LXXV (kept in iodine-free water) the dotted line of the upper graph represents the Iodothyrine series LXXX the three thin black lines and the three dotted lines in the lower graph represent each one individual of the Iodine series LXXXIX the black lines illustrating the growth of the larvae (Nos 1 2 3) which received Iodine in the form of solution and crystals as well the dotted lines representing the growth of the larvae (Nos 4 5 6) which received Iodine in the form of solution only. The amounts of Iodine administered to each larva are indicated on the bottom of the graph metamorphosis of every individual is indicated by an arrow on the growth curve.

ments, received of course far more iodine than any of the larvae that were kept in iodothyrimine

The fact that inorganic iodine alone does not effect metamorphosis of the larvae of salamanders, while its administration to the closely related tadpoles results in metamorphosis, seems to elucidate further the nature of the thyroid mechanism

On the basis of his work on the isolation and determination of the thyroid hormone, Kendall (3) has been led to conclude that iodine, although it is one of the constituents of the thyroid hormone, does not produce the "kind of reactivity" characteristic of thyroxin (the opening up of the indol ring when introduced into the body), but probably increases the "degree of this reactivity" In fact, the work of Kendall indicates, as pointed out by Kendall (4) that iodine is not split off as such from the molecule of the thyroid hormone during its action and that iodine per se is incapable of producing the effects typical of the thyroid hormone Moreover, if the hydrogen on the imino in thyroxin is replaced by acetyl, without changing the position of the iodine atoms or decreasing the amount of iodine, thyroxin becomes completely ineffective The physiologic tests on which Kendall's views are based were obtained in warm blooded animals

When it became known, however, that the administration of inorganic iodine alone to tadpoles produces the same effects as does the administration of thyroxin, Kendall (5) changed his former theory and now assumes that thyroxin has two distinct and separate physiologic functions, i e, "the effect upon the metabolic rate which is brought about by the CO-NH groups within the molecule, and the physiological changes involved in the metamorphosis of the tadpole brought about by the iodine contained in the molecule" In other words, Kendall now assigns to the iodine per se a particular function which it is able to exert also when detached from the molecule of the thyroid hormone

Before the facts brought to light by the present experiments were known to me, I held (6) the view taken lately by Kendall, the behavior of the salamander larvae, however, shows that the assumption of an independent activity of iodine is not necessary and probably even not correct and that Kendall's first view covers more closely the facts That the administration of in-

organic iodine, in some amphibian species, may result in precocious metamorphosis, does not prove by any means that iodine by itself causes metamorphosis. On the contrary, the experiments on salamanders show that inorganic iodine is quite unable to produce the structural changes involved in the amphibian metamorphosis. That administration of inorganic iodine, nevertheless, results in metamorphosis in the tadpole, while it is completely ineffective in the salamander larvae, is to be explained in the following way.

In previous work on the metamorphosis of salamanders I have been led to the conclusion that the thyroid gland of salamanders does not function during the largest part of the larval period. The excretion of a physiologically active hormone does not begin until shortly before metamorphosis, the latter phenomenon is the result of a large amount of hormone being suddenly thrown into the circulation. This is shown by various facts.

That at the time of metamorphosis the animals are suffering from severe hyperthyroidism is demonstrated by the growth curve (6). During larval life the growth is expressed by a steep and continuous line. At the time of metamorphosis, however, growth is suddenly checked and, for one or more weeks, considerable decrease in size takes place. A similar curve is produced, if metamorphosis, instead of by the animals' own thyroid glands, is caused by the administration of an excess of thyroid hormone. This suggests that at the time of metamorphosis normally a large amount of the hormone is suddenly excreted from the thyroid gland.

Second, the eyes of *Salamandra maculosa*, in order to undergo metamorphosis, need the action of the thyroid hormone, if, however, the hormone once has reached the eye, metamorphosis can be completed without the further action of the thyroid gland. During the largest part of the larval period metamorphosis of the eye can be prevented by removing the eyes to young larvae. Only if the larvae are very close to metamorphosis, removal of their eyes to young larvae does not any longer prevent metamorphosis of the grafted eyes. This fact indicates that not before a stage very close to metamorphosis is reached does the thyroid gland begin to discharge the thyroid hormone (7).

Third, removal of the thyroid gland does not interfere with

normal growth and development of salamander larvae as shown by Hoskins and Hoskins (8) This season I have extirpated the thyroid gland from several larvae of the species *Ambystoma maculatum* and so far have been able to confirm the observations made by the above named authors

Although it seems certain, from these observations, that the thyroid gland of salamander larvae does not function during the largest part of the larval period, there may be found, in the larvae of salamanders, long before metamorphosis a thyroid gland completely mature as far as total size, histological structure of the cells of the follicular walls, size of the follicles and amount and staining capacity of the colloid are concerned I have found this to be true for larvae of the species *Ambystoma opacum*, which externally did not show any indications of approaching metamorphosis and were preserved 7 weeks before the first larvae in the entire series metamorphosed Similarly larvae which do not metamorphose at all, like the axolotl larvae of the species *Ambystoma tigrinum*, possess completely mature thyroid glands as shown by Allen (9) According to this investigator, axolotl larvae possess a thyroid fully as large as the thyroid glands of normal adults of the same size, the same size and number of follicles and the same amount of stainable colloid being present in both the axolotls and the normal metamorphosed adults

It seems, therefore, that a mature condition of the thyroid and a large amount of colloid alone are not sufficient to permit of the normal function of the gland One could, of course, imagine that the colloid of the larval thyroid, in spite of its chemical similarity with the thyroid of metamorphosing animals, as shown by the affinity for dyes, is not physiologically equivalent to the active thyroid hormone This assumption, however, is probably not correct, since the investigations by Wilson and Kendall (10) as well as by Marine and his co-workers (11) have shown that the amount of active A-iodine containing principle present in a gland is directly proportional to the amount of normally staining colloid contained in the gland It seems, therefore, that in the salamander larvae the thyroid gland is able to elaborate the normal active hormone, but is unable to excrete it

In order to explain this condition I have assumed that hormone excretion in salamanders cannot take place before a certain

"releasing mechanism" (12) has developed, the action of which forces the thyroid to give up its hormone (14)

That the salamander metamorphosis is dependent on two factors, on the presence of a mature thyroid and of a peculiar releasing factor, is further suggested by the behavior of the salamander larvae when reared in low temperatures. It has been shown that the larvae of all species examined must become much larger, before they can metamorphose, when reared in low temperature, than larvae reared at higher temperatures (15). Since the development of the thyroid of the larvae kept at low temperature does not show a corresponding retardation, it seems that at low temperatures the development of a second factor necessary for metamorphosis is more retarded than growth and the development of the thyroid gland.

It is obvious from these facts that the administration of inorganic iodine could be expected to influence metamorphosis of the salamander larvae only, if inorganic iodine as such could bring about changes in the amphibian organism similar to those caused by the thyroid hormone or if the salamander larvae would possess, besides the thyroid gland, other tissues which can take up the iodine elaborate from it the thyroid hormone and excrete it without the intermediation of a particular releasing mechanism. Since, however, the present experiments definitely show that the administration of inorganic iodine does not cause precocious metamorphosis, it is obvious that inorganic iodine as such is unable to produce the structural changes involved in the amphibian metamorphosis and that, in salamanders, the thyroid is the only tissue which can elaborate, from the iodine, the thyroid hormone.

The salamander larvae are in this respect fully comparable to the mammalian organism. As shown by the athyroidous cretin iodine does not produce any effect similar to that caused by the thyroid hormone. Administration of inorganic iodine causes an effect similar to the action of thyroid hormone only in the case of a leakage of the thyroid gland, such as is found in persons suffering from exophthalmic goiter, in patients suffering from exophthalmic goiter the symptoms of hyperthyroidism are aggravated after iodine administration, because the presence of an excess of iodine leads to the elaboration and, due to the leakage of the thyroid gland, to the excretion of still larger amounts of the thyroid hormone.

And in a leakage of the thyroid apparatus, it seems to me, we must seek the explanation of the peculiar reaction of the tadpole towards the administration of inorganic iodine. For it has not been shown that in the tadpole or in any other vertebrate the inorganic iodine need not combine first with the other substances which constitute the active principle of the thyroid hormone. The present experiments show that inorganic iodine as such is unable to cause the amphibian metamorphosis. It is, therefore, much more probable that the tadpole can react on iodine administration with metamorphosis, not because of a direct action of the inorganic iodine as such, but on account of a peculiar thyroid mechanism of the tadpole. It is probable that in the tadpole organism the thyroid function has not attained a complete centralization as it has in higher vertebrates, but besides the thyroid other tissues have the ability of manufacturing the thyroid hormone. While the thyroid gland of most organisms that are in the possession of a thyroid apparatus is able to store the thyroid hormone, these tissues are unable to store the hormone after its elaboration. As Swingle (16) points out, this lack of the storage ability is the reason why an excess of iodine must be supplied to the tadpoles after thyroidectomy, in order to produce metamorphosis. It is a well known fact that, in contradistinction to the salamander larvae, the tadpoles show the effects of thyroid action very early in larval life, as indicated by the course of limb development in this group of amphibians, very probably this is due to a constant though slight "leakage" of the tadpole thyroid apparatus.

The existence of a particular releasing mechanism, as I have assumed it in salamanders, has recently been much emphasized for the thyroid of warm-blooded animals through the investigations of Cannon and Fitz (17) and of Wilson and Durante (18) and is assumed to be in this case of nervous nature. That the administration of inorganic iodine in the normal mammalian organism has no effect comparable to that of the thyroid hormone, although an excess of hormone is manufactured under these conditions [Marine and Rogoff (19)], may have its cause, too, in the action of such a releasing mechanism which under normal conditions permits only a definite amount of the hormone to escape from the thyroid gland.

In conclusion it may be said that according to these views it is impossible to test the effect of inorganic iodine as such in tadpoles, larvae of salamanders and normal warm-blooded animals. The only animal which can give an idea of this effect is the athyroidous warm-blooded vertebrate, as such an organism positively does not possess the ability of storing the iodine or combine it into the thyroid hormone. The experiments which have been undertaken on such individuals (congenitally athyroidous persons and thyroidectomized mammals) have shown, however, that inorganic iodine, if not bound to the thyroid hormone, has no effect comparable to that of the thyroid hormone. It is especially this failure of inorganic iodine to change conditions in the cretinous person, which forms the basis of Kendall's theory that iodine plays an unimportant role in the reactivity of the thyroid hormone.

The views elaborated above are in no way contradictory to the fact that nevertheless, in a biological sense, iodine is an important and essential part of the thyroid hormone, if it were possible to substitute the iodine by any other substance without changing the reactivity of the thyroid hormone, biologically this would not make iodine less important, for it is the only substance which, by the mechanism actually available to the organism, can be used in the manufacture of the thyroid hormone. Although chemically bromine or any other halogene may be able to substitute iodine without changing the chemical or even the physiological reactivity of the thyroid hormone, the organism is unable to use bromine, as shown by Swingle (20), and presumably the other halogenes to make thyroid hormone.

That iodine if supplied in excess does not produce metamorphosis of salamander larvae, does not mean, according to what has been said above, that it is not necessary in the metamorphosis of salamanders. Very likely if the larvae of salamanders would be raised on an iodine-free diet and kept in iodine-free water, metamorphosis could not take place. Nevertheless it may turn out that the salamander larvae need far smaller amounts of iodine for metamorphosis than the tadpoles do. There are certain species of salamanders (*Aneides vocans* and *Aneides lugubris*) which can complete metamorphosis without leaving the egg envelops. The larvae of these species have no opportunity to procure iodine from the outside environment.

the iodine contained in the eggs being apparently sufficient for metamorphosis. But the eggs of amphibians have never been examined as to their iodine content, it is possible that the eggs of salamanders contain more iodine than those of the tailless batrachians and that the eggs of the two species referred to above contain even more iodine than the eggs of the other salamanders.

SUMMARY

1 Administration of inorganic iodine to the larvae of the Salamander *Ambystoma maculatum* does not cause precocious metamorphosis.

2 Inorganic iodine as such is unable to produce the structural changes involved in the amphibian metamorphosis.

3 In salamanders the thyroid hormone is not excreted during the largest part of the larval period, while in tadpoles excretion of the thyroid hormone begins early in larval life.

4 This explains why the administration of an excess of inorganic iodine can produce precocious metamorphosis in tadpoles while it is completely ineffective in the larvae of salamanders.

5 In order to cause metamorphosis, iodine must combine with the substances forming the nucleus of the thyroid hormone and the rate of hormone excretion must increase with the increase of iodine available.

6 In salamanders the rate of hormone excretion is not influenced by an excess of iodine, but depends on the action of a particular "releasing mechanism."

7 There is at present no fact known, which would prove that inorganic iodine as such can function as a hormone.

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Book Reviews

A PRIMER FOR DIABETIC PATIENTS By Russell M Wilder, Ph D ,
M D , Mary A Foley, Dietitian, and Daisy Ellithorpe, Dieti-
tian, Phila & Lond , 1921 W B Saunders Co , 76 p

For review see Am J Med Sc , 1921, 162, 127

DIABETES AND ITS DIATETIC TREATMENT Ninth edition By B
D Basu, Bahadurjanj, Allahabad, 1918 Panini Office, 104 p

For review see Presse Méd , 27, 738 Conditions among
the Hindus are especially considered

DIABETES MELLITUS A SYSTEM OF DIETS [etc] By Heiman
O Mosenthal, M D , New York, 1921 Paul B Hoeber

For review see J Am Med Ass , 1921, 77, 1360

LE DIABETE SUCRE Marcel Labbé, Paris, 1920 Masson et Cie,
375 p

Reviewed in Physiol Abst , 1921, 5, 510-511

DIE LYMPHOCYTOSE Dr S Bergel, Berlin, 1921 Julius
Springer, 140 p

Though this highly interesting book is not primarily on an endocrine topic, it bears upon various endocrine problems and may, therefore, shortly be mentioned here The function of the polynuclear cells is to deal with foreign proteins, toxins or micro-organisms The function of the lymphocytes is, as Bergel has shown by most beautiful experiments, the defense against foreign lipoids Thus, tuberculous pus consists chiefly of lymphocytes because the tubercle bacillus contains a large amount of lipoids It is the same with the spirochaeta pallida and with the leprabacillus As lipoids play an enormous part in the organism the role of the lymphocytes, which prepare a lipase, is equally important In disturbances of the fat metabolism this is frequently observed and so a relation between status thymo-lymphaticus (the *thymus* and the lymph glands being the origin of the lymphocytes) and *adiposity* becomes comprehensible in this way Because the thymus has probably a more intense function in young children, these children have more lymphocytes in their blood than older individuals

The cortex of the *adrenals* has, perhaps, a certain relationship to lipid metabolism and it is remarkable that histologically it contains large numbers of lymphocytes, which have a great affinity for lipoids. Diseases of the *thyroid*, which give rise to disturbances in fat-metabolism (Graves' disease) often are accompanied by lymphocytosis. Injection of thyroïdin produces loss of fat and lymphocytosis.

Also in *diabetes*, where not only a disturbed fat metabolism may exist, but where often much fat is given with the diet, lymphocytosis is not rare. It is remarkable that lymphocytes which contain cholesterol form the *xanthoma diabetica*.

These few remarks may indicate the importance of this book not only for the biologist and pathologist, but also for those especially interested in endocrinology—J K

NUOVE IDEE SUL DIABETE ZUCCHERINO (NEW IDEAS ON DIABETES),
by Prof. Giuseppe Vigevani, Milan, 1920. Remo Sandion,
191 p.

Professor Vigevani tries to describe in this book the newer theories on diabetes mellitus and he has been able to do this in a very readable way. But it is another question whether the book must be considered as highly scientific literature. The abstractor hardly dares to give his opinion on this point, for the book is a mixture of original, interesting remarks and as many unproved statements. The author does not consider the pancreas as the only cause of diabetes. This seems, according to our present knowledge, perfectly true. His statement that no monoglandular diseases exist will not be denied by many investigators. His remark that in treatment of diabetes it is not enough to treat the glycosuria is certainly right, he states that in some cases, e.g., in cases with Graves' disease or in cases of a specific nervous character, it may even be harmful to restrict carbohydrates and that it is much better not to give animal protein. On the other hand, he considers the hypophysis as the most important organ for the regulation of growth, metabolism and sexual functions. He firmly believes that the hypophysis has an enormous importance in diabetes, the investigations of Camus and Roussy on this point are shortly and incompletely mentioned and no further notice is taken of them, the work of Leschke, who probably proved that the hypophyseal diabetes is of cerebral origin, has been overlooked. Vigevani describes even some cases which apparently have been cured (?) by administration of extracts of hypophysis.

It is amusing that in this book of new ideas nothing is said of the newer dietetic treatment, though many pages are devoted to organotherapy. The newer American and English literature on the subject has been almost entirely omitted—J K

Abstract Department

Metabolism in ADIPOSITY (Zum Fettstoffwechsel bei der Fettsucht)
Rolly (F), Deutsche med Wehnschr (Berlin), 1921, 47, 887-889,
917-919

Rolly compared the metabolism in two patients who first had been thin and later became fat. The metabolism of a patient with tuberculosis was carefully examined. I. The height was 1.67 M and weight, 56.7 K. Double castration had been done for tuberculosis of the testicles. Two and a half years after the first metabolic study he weighed 86.1 K. At this time his metabolism was again studied. When a large quantity of food was ingested the oxydations, as was proved by a study of the gaseous metabolism, were much less increased than before the operation. II. A woman with Graves' disease was treated by partial thyroidectomy. After a childbirth she became fat. While she was suffering from Graves' disease the oxydation capacity was high. After strumectomy the same change was observed as in the first patient. After childbirth she took on more weight while the oxydation capacity sank more and more. When meat was administered at the time she was thin, a marked rise in oxydation was seen. When she was stout this rise was much less marked and much slower. The administration of thyroid produced a rise in oxydation.—J. K.

Estimation of ADRENALIN in the adrenal (Bestimmung der Adrenalins in der Nebenniere) Autenrieth (W) & Quantmeyer (H), München med Wehnschr, 1921, 68, 1007-1008

Description of a colorimetric method. The adrenal is ground with sand and N/10HCl, heated to boiling and then 10% sodium acetate is added, after which it is boiled again. A solution of phosphotungstic acid and then sodium carbonate are added to the filtrate. The blue color which develops is compared with that developed from a known solution of adrenalin.—J. K.

(ADRENAL) Maligner Sympathicustumor Barnewitz Berl klin Wehnschr 1921, 58, 979

Abstracted from same article published elsewhere.—J. K.

Radiation of ADRENALS in DIABETES (Röntgenbestrahlung der Nebennieren bei Diabetes) Beumer, Berl klin Wehnschr, 1921, 58, 855

In a boy of 6½ years with severe diabetes the adrenals were submitted to x-ray treatment. The blood sugar immediately

became normal but the glucosuria and the carbohydrate tolerance did not improve. Diacetic acid and creatin disappeared from the urine, while the quantity of excreted ammonia was diminished

—J K

(ADRENALS) Formation of pigment in Addison's disease (Die Pigmentbildung beim Morbus Addisoni) Bittorf (A), *Deutsches Arch f klin Med (Leipzig)*, 1921, 136, 314-322

The pigment in Addison's disease is formed in the epithelium. In this epithelium of the skin an oxidizing enzyme (oxydase) is found capable of changing certain aromatic substances into melanins. Bittorf believes it to be a tyrosinase. Bloch believes it to be a special tyrosinase, a so-called dopa-oxydase, an enzyme, changing 3-4 dioxypyhenylalanin into melanin. This enzyme is found only in young epithelial cells. To explain the increased formation of pigment in Addison's disease, there are three possibilities: (1) More oxydase is formed, (2) those substances are formed which are oxidized into pigment, (3) a combination of 1 and 2. The author examined these theories in one case. He first found that a piece of skin from a case of Addison's disease when kept in the incubator at 37° rapidly becomes darker. In this case, however, this was not very marked and therefore he concludes that not always is there an increase in the substance the oxydation of which produces pigment. When a piece of skin from the same source is kept in a solution of adrenalin it darkens more rapidly than in other solutions. Normal skin, even when darkly pigmentated, does not become darker in a solution of adrenalin. Microscopically it is found that the epithelial cells carry the pigment. Most of it is found in the corium. Therefore it is concluded that the pigmentation is due to an increased oxydation of adrenalin in the skin. An increased quantity of oxydase is therefore probable.—J K

Unilateral ADRENAL ablation in man (Einseitige Nebennierenexstirpation beim Menschen) Boenheim (F), *Berl klin Wchnschr*, 1921, 58, 1133

Hyperacidity of the stomach contents is often found in epilepsy. After the removal of one adrenal this hyperacidity disappears. Sodium chloride is often retained in the body in epilepsy. After the removal of an adrenal the elimination of chloride is normal. It is remarkable that in epilepsy the amount of sodium chloride in the blood is low and that after the operation it becomes normal. This low content of sodium chloride in the blood as well as urine proves that it must be retained in the tissues. The carbohydrate metabolism, which is normal in epilepsy, does not undergo any change following unilateral adrenal ablation.—J K

ADRENALIN hyperglycemia (Ueber die Adrenalinhyperglykaemie)
Brösamlen, Munchen med Wehnschr, 1921, 68, 964

Adrenalin when injected into healthy persons produces an average increase in blood sugar of $\pm 0.058\%$, in most cases this rise in blood sugar does not cause glycosuria. When there is glycosuria it generally starts 3 hours after the injection and is finished within a few hours (maximum 11 hours). The hyperglycemia is observed approximately 10 minutes after the injection and reaches its maximum in about one hour. Two to three hours after the injection there is a slight hypoglycemia which is followed by a normal amount of blood sugar. The maximum increase in blood sugar is generally seen at a moment when the influence on pulse or blood pressure has already passed away. In Graves' disease the reaction of hyperglycemia is stronger than in normal persons. In thyrotoxicosis no constant changes are found, also in diabetes the reaction of hyperglycemia shows no constant features. Perhaps the study of this reaction may enable us to distinguish different types of diabetes.—J K

(ADRENIN) Roentgen-ray studies of bronchial function Bullowa
(J E) & Gottlieb (C) Am J M Sc (Phila), 1920, 160, 98-106

This study is an attempt to determine the processes by which the lungs evacuate themselves. After unsuccessful experiments with thorium in sodium citrate solution, barium in acacia and barium in gelatin, barium sulphate was triturated with anhydrous olive oil until a thick, smooth paste was formed. This paste was injected into the bronchus of an anesthetized dog. A bellows-like action in the trachea and bronchi, which may be limited by contraction of the bronchial muscles, was observed. A peristaltic action of the bronchial muscles, which seemed adequate to empty the bronchi without invoking ciliary movements also occurred. The authors in certain of these experiments injected adrenalin into dogs after filling their bronchi with barium. To their surprise, the bronchi became smaller. This same effect was observed when the injection of the adrenalin occurred before the barium. In one dog benzolbenzoate was given, this caused bronchial dilatation. Adrenalin was given and the bronchi were found contracted. In another dog bronchial spasm was induced by administering 1 mg of muscarin. An intravenous dose of adrenalin relaxed the spasm.—J F

The function of the ADRENALS (De rol der bijniere) de Caestecker, Vlaamsche Geneesk Tijdschr (Ghent), 1921, 2, 392-399

A general review without new data.—J K

Medullary malignancies of the SUPRARENAL gland with a report of cases Carter (W H), Am J Dis Child (Chicago), 1921, 22, 244

Tumors of the suprarenal cortex produce a symptomatology quite different from those of the medulla. Cortical neoplasms give rise to premature sexual development described by Bullock and Sequeira and the type in which the features are precocious obesity and muscular hypertrophy (Guthrie and Emery). Malignant neoplasms of the medulla occur only during childhood, and are of two types—the Pepper type with liver metastases and the Hutchinson type with secondary growth in the bones of the skull, sternum, vertebrae and the long bones.

Carter concludes that malignant medullary neoplasms are not unusual. In the majority of cases orbital hemorrhage is the first sign observed. Diagnosis is not difficult once the orbital hemorrhage has occurred. The disease is likely to be mistaken for trauma, chloroma or scurvy. Surgical interference can only palliate since metastases usually occur before a diagnosis can be made. Metastases probably occur in the lymph stream. The tumor rarely may metastasize to the skin. The suprarenal medulla being of neuro-ectodermic origin, the tumors resemble malignant neoplasms of the sympathetic nervous system and they are correctly designated as neuroblastoma. The article includes a report of three cases, the details of which are not of immediate endocrine interest.—M B G

The sensitiveness of the human organism to ADRENALIN (Zur Frage der Adrenalinempfindlichkeit des menschlichen Organismus) Csépai (K), Deutsche med Wchnschr (Berlin), 1921, 47, 953-954

When 1 mgm of adrenalin is injected subcutaneously the blood pressure rises. The way in which this develops—the rapidity and the intensity—have been considered by some authors as a method for diagnosis of the irritability of the involuntary nervous system. Csépai, however, points out that the effect of a subcutaneous injection is not in the first place due to the rapidity of absorption. He therefore injected very small quantities (0.01-0.04 mgm) adrenalin intravenously. He often observed cases in which there was no increase in blood pressure after subcutaneous or intramuscular injection of adrenalin but in which there was a normal rise after intravenous injection. Only in dying persons no reaction is seen. The difference seen after subcutaneous injections in different persons is a simple difference in absorption and has no relation whatever to the irritability of the voluntary nervous system.—J K

ADRENAL and antigens (Nebenniere und Antigene) Emmerich, Berl klin Wchnschr, 1921, 58, 556, Deutsche med Wchnschr (Berl), 1921, 47, 666

Human adrenals may be valuable as antigens in the Wassermann test when they contain enough lipoids. The best antigen is made from adrenals from patients with arteriosclerosis, in cases of

tumors, scarlet fever or acute yellow atrophy of the liver the adrenals are not always fit for preparing antigens. The adrenals of horses are valuable for preparing antigens for the Wassermann test and the flocculation test of Sachs and Georgi —J K

(ADRENAL) Ether hyperglycemia and glycosuria on the rabbit
Fujii (I), Tohoku J Exper M (Sendai), 1921, 2, 169-208

The author, using rabbits as subjects, investigated the effect on ether glycosuria and ether glycemia of (1) depth of anesthesia, (2) changes in body temperature, (3) bilateral splanchnectomy, and (4) variation in adrenal secretion. The latter was determined by the difference in degree of staining of the two adrenals after ether anesthesia preceded by a unilateral splanchnectomy. He noted that the degree of ether hyperglycemia and glycosuria was roughly proportioned to the depth of anesthesia. Ether hyperglycemia occurred in animals whose body temperature was maintained at normal. If the temperature were allowed to fall the hyperglycemia increased. Bilateral splanchnectomized animals developed some hyperglycemia from ether anesthesia. Rabbits with unilateral splanchnectomy developed the same degree of ether hyperglycemia as normal animals. The chromophil substance in the adrenal on the side of the cut splanchnic always stained more deeply than the other —E L R

Treatment of paralysis of the heart in narcosis with intracardial injections of ADRENALIN (Bekämpfung des Narkose-Herzstillstandes durch intrakardiale Adrenalininjektion) Frenzel (H), München med Wchnschr, 1921, 68, 730-732

In many cases the injection of 0.1 cc of a 1% solution of adrenalin into the heart gave good results —J K

(ADRENIN) Comparative examination of arterial, capillary and venous blood in man (Vergleichende Untersuchungen am arteriellen, kapillaren and venösen Blut des Menschen) Hesz (O), Deutsches Arch f klin Med (Leipzig), 1921, 137, 200-224

Comparative examination of the blood in arteries, veins and capillaries of the forearm has shown that normally the venous and capillary bloods contain the same quantity of erythrocytes, while the arterial blood often contains a greater number. Heart lesions seem to result in an increased number of erythrocytes in the capillaries. Artificial venous stasis is followed by an increase of erythrocytes in veins and capillaries and a decrease in the arteries. Hesz has endeavored to find out whether the rise in blood pressure following injection of adrenalin causes a change in blood concentration. He finds that the number of corpuscles in arteries and veins is increased, in the capillaries, however, it is diminished. Often

the maximum number of corpuscles and the maximum blood pressure are not synchronous. Therefore it is concluded that the changes in concentration are not due to the changes in blood pressure—J K

(ADRENIN THYROID) The Goetsch test (L'épreuve de Goetsch) Garnier (M), & Bloch (S) Bull et mém Soc méd d Hôp de Par, 1921, 45, 1137-1142

A report of the application of the Goetsch test to 48 patients. Out of the group 16 gave a definitely positive reaction, 10 gave a weakly positive reaction and 22 were negative. Among the cases which failed to react were 3 with Basedow's disease, and 2 with myxedema. In cases of transitory hyperthyroidism the reaction is not given after the disturbance has subsided—F S H

Intracardial injection of ADRENALIN and strophanthin in acute cardiac paralysis (Intrakardiale Einspritzung von Adrenalin-Strophantin bei akuten Herzlähmungen) Guthmann (H), München med Wchnschr, 1921, 68, 729-730

The author recommends the injection of 1 mgm adrenalin and 1 mgm strophanthin into the heart in acute cardiac paralysis. In all cases in his experience the heart began to beat again. In 3 patients that died no changes were seen in the heart at autopsy—J K

Suggestions for the Austrian Pharmacopœia IX Adrenalin Heisler (R), Pharm Post, 1918, 51, 677-678, Chem Zentralbl, 1919, 2, 208-209

H demands an absolutely colorless adrenalin solution. Brown, red or cloudy solutions are to be rejected, while faintly rose-colored are permissible. The acidity limit should be fixed at 0.25 cc 0.1 N NaOH per 5 cc of 1% adrenalin solution, methyl orange being used as indicator—Chem Abst, 13, 2730

The influence of ADRENALIN on the blood picture (Zur Beeinflussung des Blutbildes durch Adrenalin) Hoefel (G A) & Herzfeld (E), Folia haematologica (Leipzig), 1921, 27, 77-95

In normal subjects injection of adrenalin is generally followed by changes in the numbers of leucocytes. First there is a marked lymphocytosis with a more or less intense increase in neutrophil cells. Then the number of lymphocytes sinks, often below normal, with a slight increase in polynuclear cells. In rare cases a third phase with marked leucocytosis and slight lymphocytosis is observed. In a case of pernicious anemia without pathological cells in the blood (the only morphological symptoms in the blood being aniso- and polikilo-cytosis), normoblasts and basophil punctuated cells came into the circulation after injection of adrenalin. In the

same way in a case of "pseudobanti" myelocytes, which had not been found before, appeared in the circulation In a case of acute myeloid leucemia first the polynuclear cells showed an enormous increase Then their number went down, to rise after this for a second time The small number of leucocytes and the myelocytes also showed an increase —J K

The white ADRENAL line (Sergent), its clinical significance Kay (W E) & Brock (S), Am J M Sc (Phila), 1921, 191, 555-561

From a study of a series of 255 cases of a variety of diseases and normals upon which numerous pharmacologic and other tests were performed, the authors conclude that the so-called white adrenalin line of Sergent is a local vasomotor reflex, resident in the skin, bearing no direct relationship to adrenal gland activity They give as their reasons its independence of blood-pressure, acute fatigue, and other signs of hypoadrenia, its frequent occurrence in normals and in a variety of diseases unassociated with hypoadrenia, its reappearance in the face of persistent general manifestations of adrenalin subcutaneously administered, its peculiar association with scarlet fever It would appear that the state of the vasomotor system which allows of its best exhibition is found in young adults of either sex, and especially in the exanthem of scarlet fever On the basis of this series it is stated that this line has not the clinical significance attributed to it —J F

Tuberculous ADRENAL in Addison's disease (Tuberkulose Nebenniere bei Morbus Addisoni) Kraus (E T), Berlin klin Wchnschr, 1921, 58, 1086

In a case of Addison's disease with tuberculosis of an adrenal the pancreas was much atrophied This supports the theory of Falta, that there exists an antagonism of pancreas and adrenal —J K

Tuberculosis of ADRENAL (Tuberculose einer Nebenniere) Kraus (E T), Wiener klin Wchnschr, 1921, 34, 518

In a case of Addison's disease a tuberculous adrenal was found, with a marked atrophy of the pancreas —J K

ADRENALS and Epilepsy Kutschera (L), Deutsche med Wchnschr, Berlin, 1921, 47, 1282

In two cases of epilepsy the author removed the left adrenal The effect was only temporary —J K

(ADRENIN) Urticaria, classification of types and its causes Lambright (G L), Am J M Sc (Phila), 1921, 162, 183-187

In this paper, the author incidentally reports a case of urticaria following injection of foreign protein (antidiphtheritic serum) which

adrenalin relieved entirely, but it soon reappeared and lasted for several days —J F

(ADRENAL) Pathology and histology of Addison's disease (Zur pathologischen Anatomie und Histologie der Addisonschen Krankheit) Lubarsch, Berlin klin Wchnschr, 1921, 58, 1195

A short note Addison's disease is often complicated by status thymolymphaticus In this case there was no tuberculosis, but a very marked status thymolymphaticus even including the thyroid

El tratamiento del asma bronquial por la ADRENALINA en inyecciones hipodérmicas e intramuaculares Rev med-quir (Tegucigalpa, Honduras), Maira (O), 1919-20, 1, No 4, 6-14, Anales Fac d med de Montevideo, 1919, 4, 515-531

Maira reiterates that many years of experience have convinced him that epinephrin is the treatment par excellence for combating attacks of asthma These patients stand large doses One had suffered from asthma for fifteen years when subcutaneous injections of epinephrin were begun in 1914, with prompt relief for several hours The dose was 15 drops, and it was repeated twice and sometimes three or four times a day This has been kept up for five years, with more than 300 injections, and no by-effects have been observed Maira has seen nothing to indicate that epinephrin brings on arteriosclerosis when given by subcutaneous or intramuscular injection The latter is preferable when rapid action is desired He has obtained good results with it also in whooping cough —J Am M Ass

(ADRENIN) Blood volume and blood volume methods, Lamson (P D) & Nagayama (T), J Pharmacol & Exper Therap (Balt), 1920, 15, 331-346

After injection of adrenin (0.9 mgm per kilo) there is an increase in red cell concentration and a decrease in plasma volume, an actual loss of fluid into liver lymphatics, for if the liver is previously removed there is no change in red cell concentration

—F A H

The influence of ADRENALIN on the voluntary muscles (Die Wirkung des Adrenalins auf die Skelettmuskulatur) Lange, Wien klin Wchnschr, 1921, 54, 386

Adrenalin diminishes the permeability of the sarcolemma and alters the irritability of the voluntary muscles (No details are given) —J K

Influence of glands with internal secretion on the respiratory exchange II Effect of SUPRARENAL insufficiency (by removal or by freezing) in rabbits Marine (D) & Baumann (E J), Am J Physiol (Balt), 1921, 57, 135-152

Rabbits display a wide variation in the duration of life following double suprarenal ablation, and it is thus possible to get a graded series for metabolic studies. Observations were made at 2 hour intervals, after control metabolic rates had been established for several weeks. Respiratory exchange was determined by the modified Haldane apparatus. The conclusion is that removing or crippling (by freezing) the suprarenals results in a metabolic disturbance, characterized by increased heat production and CO₂ output, definitely related to the completeness of removal of the cortical function. The symptom complex somewhat resembles that of exophthalmic goiter.

—T C B

L'ADRENALINE dans le choléra Naamé, Gaz de Hôp, civ et mil (Paris), 1921, 94, 678-679

The author cites evidence that has convinced him that the symptomatology of cholera is to be ascribed to adrenal deficiency. The deduction is based on the allegations that the suprarenal glands in cholera show characteristic degenerative lesions and that adrenin has remarkable curative effect in this disease.—R G H

The calcium ion as an antagonist of ADRENIN (Het calcium ion als antagonist van adrenaline bij vaat doorstroming en bloedsdruk)
Noyons (A K), Nederl Tijdschr v Geneesk (Haarlem), 1921, 65 (II), 793-794

The experiments were carried out on rabbits with a cannula in the abdominal aorta and a cannula in the inferior vena cava. When calcium is added to the solution the vasoconstricting effect of adrenin is decreased. When, however, a calcium salt is added and at the same time sodium acetate, no influence of this mixture is seen on the activity of adrenin. When an animal repeatedly gets injections of calcium chloride, until the amount of calcium in the blood is larger than normal, adrenin does not produce a rise of blood pressure. When, however, in such an animal citrate of sodium is injected, adrenin again has its ordinary effect on the blood pressure. Either calcium or adrenin alone has a vasoconstricting action. Together, however, they neutralize each other.—J K

(ADRENIN) Vascular reactions in vascular hypertension O'Hare (J P), Am J M Sc (Phila), 1921, 159, 369-380

This is a study of the effects of rest, excitement, nitroglycerine, and adrenalin upon patients with high-blood pressure and normal renal function. The observations were carefully made. Adrenalin, 0.5 cc of 1:1000 solution, was given intramuscularly after the normal base line for the blood pressure had been determined. Frequently readings were taken then until the pressure returned to this base line. It was shown that in this type of case the vessels were especially sensitive to adrenalin, a marked rise in pressure—often an

alarming one—taking place immediately after its injection, intramuscularly —J F

EPINEPHRIN hypersensitiveness and its relationship to hyperthyroidism Peabody (F W), Sturgis (C C), Tompkins (E M) & Wearn (J T), *Am J M Sc* (Phila), 1921, **161**, 508-517

From the application of the Goetsch test to a series of patients, these workers conclude that different individuals, both sick and well, react with different degrees of intensity to the injection of epinephrin and that the fundamental nature of the reaction is unknown. But it seems probable that it is due to a stimulation of the sympathetic nervous system. Therefore, there would be no reason for assuming that a positive reaction is constantly associated with hyperthyroidism. The "positive" reaction is frequently associated with this disease, but not always. It is also found in many psychoneurotics, in about 50 per cent of patients convalescent from acute infection, in about the same proportion of soldiers with "effort syndrome," and in 14 per cent of apparently healthy young medical students —J F

ADRENAL tuberculosis and biliary lithiasis (Tuberculosis supracapsular y litiasis biliar) Raverot (M) & Bacigalupo (J), *Semana Méd* (Buenos Aires), 1921, **28**, — — (No 17)

Post-mortem examination in a young girl showed tubercular destructions of the adrenal capsules. A calculus was found in the gall duct —B A H

ADRENALIN and anti-pneumococcic serum injection in primary pneumopathies for provocation of the crisis (Provocation de la crise salutaire dans les pneumopathies primitives par l' injection intraveineuse de sérum antipneumococcique et d' adrénaline Statistique, résultats Interpretation) Renaud (M), *Bull et mém Soc méd d hôp de Par*, 1921, **45**, 919-927

Renaud reports a mass of data from some 750 cases of pneumonia in many of which he provoked the crisis by the intravenous injection of 0.5 mgm of adrenaline in combination with anti-pneumococcic serum. He considers his results justify the use of the drug in such cases —F S H

The preparation and preservation of ADRENALIN solutions Richard (F) & Malmy (M), *J pharm chim* (Paris), 1921 (7), **23**, 209-214

The adoption of an official solution of adrenalin (1:1000) is urged because of the great variations in the formulas of the solutions sold at present. Tests show that solutions made by the aid of SO₂, with physiological salt solution as base, are best, the SO₂ acts as solvent, antiseptic and preservative. The adrenalin is dissolved in

100 cc of physiological salt solution (7.5 gm NaCl per l) containing 10 gm SO_2 per l (controlled by back titration with 0.1N I_2), and brought to 1000 cc by the addition of sterilized physiological salt solution. This solution must be made in the absence of NH_3 fumes. If preserved in ampoules, filled in an atmosphere of CO_2 , it has been kept a year —Chem Abst, 15, 2335

(ADRENAL) A case of Addison's disease treated with success by tuberculin (*Enfermedad de Addison tratada con éxito por la tuberculina*) Saez de Santa Maria (R.), Méd Ibera (Madrid), 1921, 14, 19-21

Clinical history of a patient with Addison's disease whose primary symptoms appeared after an attack of typhoid. The treatment consisted of opotherapy combined with tuberculin in progressive doses, following which occurred marked improvement. After four years' observation, says the author, the patient was able to consider himself clinically cured —E B

Treatment of epilepsy by removal of an adrenal (*Zur Behandlung von Krämpfen mit Exstirpation einer Nebenniere*) Sándor (S.), Zentralbl f Chir (Leipzig), 1921, 48, 881-883

Although the author operated in 4 cases the time elapsed is still too short to speak of definite results. Nevertheless, this operation may be tried in cases in which other treatment has failed —J K

ADRENAL insufficiency (*Formes cliniques et traitement de l'insuffisance surrénale*) Sézary (A.), Presse méd (Par), 1919, 27, 533-535

Sézary classifies suprarenal insufficiency under three headings: the fulminating, rapidly fatal form, the monosymptomatic form (myasthenia or amyotrophy), and the form inducing a whole set of symptoms: acute (syndrome of Sergent-Bernard), subacute and slow (Addison's disease and its varieties). Tuberculosis may induce any one of these "syndromic forms" of suprarenal insufficiency, and syphilitic processes often locate in the suprarenals, as also those of diphtheria, typhoid and other acute infections. Specific treatment should be given when such is possible, antitoxin with diphtheria, for example, or quinin with malaria. Rest and suprarenal treatment are useful whatever the infection, but he prefers the extract of the whole gland, and given by the subcutaneous route. He reserves epinephrin for acute disturbances with collapse of the heart, and recommends the subcutaneous route. He gauges the dose by the therapeutic results obtained with the first doses and by the signs of intolerance. A rise in the blood pressure is a good index of the efficacy of the opotherapy, but the fact that it does not rise does not prove that the treatment has been ineffectual. A still more instructive index is the finding with the dynamometer showing the variations in the strength

of the muscles tested fifteen and thirty minutes, one hour, three hours and so on after the injection of the suprarenal extract. When these two tests show a favorable influence from the suprarenal treatment, he keeps up this dose, not increasing it until the effect grows less pronounced. The appearance of tremor calls for caution, glycosuria, albuminuria, circulatory disturbances require suspension of this treatment. In some cases the doses have to be high and kept up for several weeks or even months before a good result is obtained. Signs of intolerance should be watched for with special care in these circumstances. Sometimes addition of pituitary will give surprisingly fine results when the suprarenal treatment is a failure. With cheesy tuberculosis and cancer, the knife is still the ideal treatment, possibly resecting only the pathologic tissues and leaving the rest intact. But in order that this can be done the disease has to be diagnosed early, and it is to be hoped that the progress of medicine will soon render this possible—*J Am M Ass*, 73, 1399

ADRENAL ablation in the treatment of genuine epilepsy (*Die Nebennierenreduktion in der Behandlung der genuine Epilepsie*) Steinthal (C), *Zentralbl f Chir* (Leipzig), 1921, 48, 878-881

A report of seven cases operated upon without successful outcome. After the operation the blood pressure, blood picture, NaCl metabolism, carbohydrate tolerance, blood sugar and bilirubin content of the serum were unchanged. The acidity of the gastric secretion appears to have been slightly lowered—*J K*

Is ADRENAL ablation justified in epilepsy (*Ist die Nebennierextirpation bei Epilepsie berechtigt?*) Specht (C), *Zentralbl f Chir* (Leipzig), 1921, 48, 1347-1348, *Deutsche med Wchnschr* (Berlin), 1921, 47, 1313

When animals are inoculated with tetanus toxin fatal spasms occur which are identical whether one adrenal is removed or not. Fischer has stated that the removal of one adrenal diminishes the sensibility of animals towards amyl nitrite. As the animals show great individual differences in sensibility, Specht first estimated this sensibility before and after removal of an adrenal. Perhaps some small changes, but certainly no important increase of the resistance was observed. But even if Fischer's statements were true, the operation would be useless in epilepsy, since not only does the other adrenal show hypertrophy, but also the residue of the chromophil tissue may also enlarge—*J K*

Epinephrin hyperglycaemia II Tatum (A L), *Pharmacol & Exper Therap* (Balt), 1921, 18, 121-131

A study of the conditions under which epinephrin acts as a glycogenolytic agent. Epinephrin, as a glycogenolytic agent, has only

a transient existence in the circulating blood Epinephrin glycolysis occurs only *pari passu* with the inflow of epinephrin into the blood, be it from subcutaneous or from direct injection There is no essential difference between the glycogenolytic action of epinephrin given intravenously and given subcutaneously —J B C

Need of the physiological control of ADRENALIN and of preparations of the suprarenal glands Tiffeneau (M), *J pharm chim (Paris)*, 1921 (7), 23, 313-317, 366-375

A plea for the physical, chemical, and biological control of adrenalin and its preparations based on the variable results noted on testing, by a modified U S P method, 5 commercial adrenalin solutions, and 5 preparations of the suprarenal glands —Chem Abst, 15, 2336

ADRENAL ganglioneuroma with testicular hypertrophy [Ein Ganglioneurom der Nebenniere (mit Hodenhypertrophie)] Wassmund (C), *Virchow's Arch f path Anat [etc]* (Berlin), 1919, 226, 319-332

Wassmund found in the medulla of the right suprarenal of a man, aged 26, a tumor the size of a walnut, composed of sympathetic ganglion cells and nerve-fibres, medulated and non-medulated, which were tending to infiltrate the cortex of the gland —Med Sc Abst & Rev, 5, 40

(ADRENIN, THYROID) Sensitization for radio-activity by hormones (Sensibilisatie voor radioactiviteit door harmonen) Zwaardemaker (H), *Nederl Tijdschr v Geneesk (Haarlem)*, 1921, 65 (II), 794-796

When the potassium is removed from Ringer's solution used to perfuse a frog's or mammal's heart, it ceases to beat If potassium or another radio-active salt (uranium, radium) is added or exposure to radium rays is made, the heart again beats The "radio-biological" dose was found to be much smaller during summer than during winter He observed that the sensitivity to radio-activity is decreased by calcium, strontium, barium and perhaps thyroidine It is increased by fluorescein, eosin, choline and adrenin In summer 5 mgm KCl to one litre of Ringer's solution must be present to make the heart beat When, however, 0.001 mgm of adrenin is added only 1 mgm KCl is needed The same amount of adrenin lowers the summer dose of uranium nitrate from 0.1 to 0.01 mgm per litre It is possible that the hormones are the regulators of the potassium radio-activity in the body —J K

The importance of the AUTONOMIC nervous system in clinical medicine (De beteekenis van het vegetatieve zenuwstelsel voor de kliniek) Koopman (J), *Handelingen van het XVIII de Neder-*

landsch Natuur en Genneeskundig Congres (Haarlem), 1921, 18, 146-148

A general review without new facts —J K

The pharmacology of the AUTONOMIC nervous system Storm van Leeuwen, Handel v h XVIII d Nederl nat-en geneesk Cong (Haarlem), 1921, 18, 148-151

A critique on the theory of *vagotonia* and *sympathicotonia* according to Eppinger and Hess The sensitivity of animals to pilocarpin, atropin, histamin and adrenalin is not at all changed after extirpation of pancreas, thyroid or adrenals It is generally accepted that adrenalin stimulates the ends of the sympathetic, pilocarpin the myoneural junctions of the vagus It has, however, never been proved that these substances have any relation to these nerves If, in the book of Eppinger and Hess, every "*vagotonia*" is changed into "*sympathicotonia*" and every "*sympathicotonia*" into "*vagotonia*," the conclusions are just as logical as in the original version Nearly all persons who have a special sensitivity to adrenalin have practically the same to pilocarpin It is perhaps possible that there exist patients who have all the symptoms of *vagotonia*, but all the relations between these symptoms and the functions of adrenals or thyroid have not yet been proved The pharmacological way of diagnosing *vagotonia* seems to be perfectly useless —J K

(TETANY) The importance of the calcium-ion concentration for the existence of spasmophilic symptoms (De beteekenis van de concentratie van vije calciumionen voor het ontstaan van spasmophile verschijnselen) Van Paassen (P), Nederl Tijdschr v Geneesk (Haarlem), 1921, 65, 1162-1171

It is a fact, admitted by all investigators, that calcium plays an important part in the pathogenesis of tetany The total amount of calcium present in the blood is not as important as is the quantity of free calcium, which is intimately related to the irritability of the nervous system This concentration depends mainly on the concentration of the bicarbonate-ions When the total amount of calcium increases $\text{Ca}(\text{HCO}_3)_2$ is formed which gives rise to a momentary decrease of concentration of bicarbonate-ions The determination of the total of free calcium-ions is advocated as a clinical procedure When the concentration of Ca-ions is decreased nervous irritability rises, though a real attack of tetany has never been observed in the author's experiments Calcium is certainly not the only important factor in the pathogenesis of tetany —J K

(CORPUS LUTEUM) Experimental studies of oval implantation and development in the uterus (Experimentelle Studien über die Einnistung und Weiterentwicklung des Eis im Uterus) Biedl

(A), Peters (H) & Hofstätter (R), Ztschr f Geb s u Gyn (Stuttgart), 1921, 84, 59-130

This is a noteworthy contribution to the subject of the implantation of the egg and its development within the uterus Its length and detail preclude an adequate abstract The observations indicate that the corpus luteum may participate in the phenomenon —F S H

Experimental studies in DIABETES Series II The internal pancreatic function in relation to body mass and metabolism II Changes in assimilation by alteration of body mass III The effects of exercise IV Pancreatic cachexia Allen (F M), Am J M Sc (Phila), 1921, 161, 16-32, 165-193, 350-364

In considering the second paper of this series these relations were investigated in obese dogs, by a study of the alteration of body weight in the same animal and the alteration in the body mass in the form of active protoplasm The conclusions drawn are that the assimilative power of diabetic animals rises and falls inversely with the body weight This change is established on different diets, which excludes the supposition that it is due merely to variations in either glycogen or protein, and which proves that it is produced also by the feeding and deposit of a non-sugar forming material, namely, fat When considerable masses of active tissue, especially muscle, are removed by amputation, the effects upon the assimilation are negligible compared with those of similar losses of weight produced by undernutrition It may therefore be concluded that the effects of undernutrition are not due to a reduction of active protoplasm but rather to a reduction of food supplies and metabolism The pancreatic function is spared when the same number of cells metabolize a reduced quantity of food materials This principle is important clinically in that undernutrition should be continued to the point of relieving the pancreatic function from overstrain revealed by the most delicate tests, particularly hyperglycemia The present investigation has aimed at the valid proof of a quantitative relation between the internal pancreatic function and the total body weight and metabolism Any theories of the nature of this function or of diabetes must take account of the fact that the islands of Langerhans are concerned not merely in the combustion of sugar or storage of glycogen, but also in the maintenance of the general tissues and reserves In some manner an increased supply of fat or formation of adipose tissue imposes a burden on the island function, and reduction of any kind of food or of the body weight reduces the demand upon this function This fact seems to indicate that the island hormone has both a catabolic and an anabolic role

In the third paper of this series the influence of carbohydrate assimilation was traced from the normal through various stages of impairment A rise of plasma sugar, presumably representing increased transportation, ordinarily accompanies exercise in the normal

animal, and the assimilation for test doses of glucose is increased. In mild diabetics, when there is a tendency to abnormal hyperglycemia from defective assimilation of carbohydrate, exercise markedly diminishes the hyperglycemia and glycosuria and facilitates utilization. This power of exercise to improve assimilation applies to the glucose formed from protein diets or body stores as well as from preformed carbohydrate. It does not depend upon the febrile temperatures which attend heavy exercise in dogs, for equal results were obtained in human patients without important elevations of temperature. It is not lost with long usage, but becomes less as the diabetes becomes more severe. At a certain advanced stage exercise is unable to modify hyperglycemia or glycosuria. Beyond this, in the extreme forms of diabetes in partially depancreatized animals and in totally depancreatized animals, the extra mobilization of sugar by exercise results in an actual increase of glycosuria and of the D N ratio.

In the clinical application, dependence for the actual control of the diabetes is placed upon diet, and exercise is limited to the requirements of comfort and hygiene. The thorough dietetic treatment thus involves two changes from former practice: on the one hand heavy exercise as advocated by the earlier clinicians for burning up surplus sugar is discouraged, on the other hand, the hygienic benefits of lighter exercise are made available to many patients to whom exercise was formerly forbidden.

Continuing this in the fourth paper, Allen reports his observation on the acute deaths from unknown cause after partial pancreatectomy. Examples of diabetic asthenia, diabetic gangrene in animals as well as examples in which the diabetes of dogs and cats was replaced by a fatal cachexia of unknown origin are given. He considers the diabetic asthenia and gangrene as due to specific endocrine deficiency. He emphasizes the importance of distinguishing mere suppression of glycosuria by some injury, poison, or cachexia, from genuine control or improvement of the diabetes.—J F

The management of certain types of DIABETES MELLITUS Branton (W B), Virginia Med Mo, 1921, 48, 267-271

The author points out that diabetes mellitus should be recognized by the routine examination of the urine and the blood for sugar before symptoms arise. He calls attention to the faint yellow reactions got in doing Fehling's test on mild diabetics. Some of the problems of handling the obese diabetic are pointed out. The usual method of rendering such cases sugar free is shown. The difficulty of reducing such a patient's weight, the seriousness of a persistent ferric chloride reaction, and the level to which one should attempt to reduce the blood sugar often present unanswerable problems. The difficulty of treating diabetes complicated by tuberculosis is dwelt upon. Allen's treatment was used in four cases, the results were

not encouraging Finally, old age should not debar any patients from the benefits of modern dietetic treatment They should be rigidly kept to their allowance of food, though all changes in their former habits should be made slowly and with extreme care Cases illustrating each point are reported—Author's Abst

Atropin in DIABETES (Atropin bei Diabetikern) Bornstein (A),
Deutsche med Wchnschr (Berlin), 1921, 47, 1200-1201

Substances which stimulate the parasympathetic increase the quantity of blood sugar This has been proved for pilocarpin, physostygmín, cholin and acetylcholin When atropin is first given these substances have no effect In about 25 per cent of the cases of diabetes, atropin causes a decrease of blood sugar—J K

DIABETIC acidosis Edgar (T W), Med Rec (New York), 1921,
99, 952-954

The author is not an enthusiastic advocate of the starvation treatment in diabetes mellitus, believing that many patients become too undernourished, weak, and economically unfit He does not seem to consider "getting the urine free from sugar" the goal to be striven for in most cases "Many patients are worse off with a sugar free urine than others whose sugar content is high" His treatment for acidosis is then outlined, depending upon whether the patient is in coma or not Essentially it consists in the administration of carbohydrate by mouth or as glucose per rectum or intravenously, together with alkalis In the treatment of diabetics, body weight should be preserved unless, of course, the patient is obese He believes the thin and cachectic develop acidosis more readily He has never seen one gaining or maintaining his weight develop coma
—H L

(DIABETES) Alimentary hyperglycemia and glucosuria (Zur alimentaren Hyperglykämie und Glycosurie) Eisner (G) & Forster (O), Berl klin Wchnschr, 1921, 58, 839-842

Hyperglycemia may exist without glucosuria, glucosuria may exist without hyperglycemia The explanation that in these cases the kidney is more or less permeable for sugar is no explanation, but simply states the problem in other words The authors give 150 grams of white bread to many persons when fasting The blood sugar frequently rises about 100 per cent on this diet Here a most interesting fact was observed In one patient 100 grams of saccharose was given on the empty stomach The blood sugar rose from 0.115% to 0.186% and glucosuria occurred In the same patient the injection of 1 mgm of adrenalin caused a rise of the blood sugar to 0.2% with glucosuria After 100 gm of wheat flour and 100 gm of white bread the blood sugar rose to 0.18%, but no glucosuria was observed

It is often possible to obtain by bread feeding the same amount of blood sugar as by the injection of adrenaline. In the first case, however, no glucose is found in the urine, while in the second glucosuria is quite common. The greatest increase in blood sugar after administration of bread is seen in persons with an increased irritability of the involuntary nervous system or in patients with a hyperfunction of the chromophil tissue. Often the rise of the blood sugar begins as soon as the first pieces of bread have only just been ingested. The authors suggest that in these cases a nervous impulse from the stomach goes to the liver, which then mobilizes the sugar. If this is true, alimentary hyperglycemia may be compared to piqure hyperglycemia. We know nothing about the relation between hyperglycemia and glucosuria. It is, however, probable that the occurrence of glucosuria depends on the intensity of the rise of the blood sugar and on its duration.—J K

(DIABETES) Phosphates and blood sugar (Phosphatinjektion und Blutzucker) Elias (H) & Weiss (St), Berl klin Wchnschr, 1921, 58, 959-960

In normal persons intravenous injections of solutions of NaH_2PO_4 or Na_2HPO_4 had no influence whatever on the blood sugar, though they decreased alimentary hyperglycemia. In diabetics hyperglycemia was nearly always diminished by these injections. It was possible to prove that the sugar was not excreted in another way, for instance as levulose-biphosphate.—J K

Practical and historical observations on the "Mehlfruchtcur" in DIABETES mellitus (Praktisches und Historisches zur Mehlfruchtcur bei Diabetes mellitus) Falta (W), Deutsche med Wchnschr (Berlin), 1921, 47, 889-891

Falta calculates that 100 grams of protein may produce about 80 grams of sugar. It is, therefore, possible to give the quantity of allowed food, partly as protein and partly as carbohydrates when the tolerance for carbohydrates is known. In cases with acidosis more carbohydrate, in other cases more protein must be given. Not all proteins and not all carbohydrates can be given with the same success. Generally when small quantities of protein are given an increased amount of fat in the diet has no influence on the excretion of sugar or fat. There are patients with diabetes who have a special sensibility against proteins, others are very sensitive towards carbohydrates. A diet rich in calories but poor in proteins should be tried.—J K

Retention of protein during diet reduction to relieve the glycosuria in DIABETES MELLITUS Fenlon (R L), Am J M Sc (Phila), 1921, 161, 193-203

Fenlon now reports forty cases treated by this method and outlines the details of the method and instructions together with illustrative case histories. It consists essentially of maintenance of the protein intake at a moderate level, restriction of fat and relatively rapid reduction of carbohydrate until the patient's glycosuria disappears. The carbohydrate tolerance is then built up by a gradual increase in the carbohydrate intake —J F

Studies on blood sugar The total amount of circulating sugar in the blood in **DIABETES** mellitus and other conditions Fitz (R) & Bock (A V), J Biol Chem (Balt), 1921, 48, 313-321

The plasma of blood from diabetic persons contains relatively more sugar than do the corpuscles. This suggests that the plasma in diabetes is a vehicle for the transportation of sugar from the body cells, which are unable to burn or store it, to the kidney which excretes it, and that the blood corpuscles are but little concerned with such transportation of sugar. Glucosuria does not occur unless the plasma sugar exceeds a certain threshold. Blood sugar concentration expressed as milligrams per 100 cc of blood or plasma may give misleading information with regard to the total amount of circulating sugar. The threshold at which glucose appeared in the urine of the diabetic patient of this series seemed to lie between 5.20 and 5.36 grams of total plasma sugar —F S H

(DIABETES) Symptoms and treatment of coma diabeticum (Symptomatologie und Therapie des Coma diabeticum) Forschbach (J), Ztschr f ärztl Fortbild (Jena), 1921, 18, 421-427
A general review without new data —J K

The administration of roasted carbohydrates to patients with DIABETES (Ueber die Ernährung von Zuckerkranken mit stark gerosteten Kohlehydraten) Grafe, Deutsche med Wchnschr (Berlin), 1921, 47, 1080

Data reported elsewhere —J K

Feeding DIABETICS with roasted carbohydrates (Die Ernährung der Diabetiker mit gerosteten Kohlehydraten) Grafe (E), München med Wchnschr, 1921, 68, 827-829

Grafe points out that, as caramel may be of great use in the treatment of diabetes, it was desirable to try roasting of other carbohydrates. It is possible by adding much fat to make tasteful food from roasted rice, potatoes, porridge, oats, bread, etc. The glucosuria, produced by these substances, is four to ten times less after than before roasting —J K.

(DIABETES) The apparent influence of a diet of carbohydrates on the pancreas remnant of partially pancreatectomized dogs Jensen

(V W) & Carlson, (A J), *Am J Physiol* (Balt), 1920, 51, 423-429

After the removal of approximately 88% of the pancreas gland a liberal carbohydrate diet tends to change diabetes levis into diabetes gravis. The authors question the soundness of the theory that fasting relieves diabetes in man by removing "overstrain" from an impaired pancreas. There was practically no hypertrophy of the pancreas remnant when its functional capacity had been reduced to a point below its ability to prevent diabetes—Chem Abst

Formation of antibodies and INTERNAL SECRETION (*Vorming van tegenstoffen en inwendige afscheiding*) Koopman (J), *Nederl Tijdschr v Geneesk* (Haarlem), 1921, 65, 3489-3495

A review of the literature on this subject. No new data—J K

DIABETES und Chirurgie Krecke (A), *München med Wchnschr*, 1921, 68, 887-888

A general review. When an operation is absolutely necessary (ileus, hernia incarcerata) diabetes should not be regarded as a contraindication, but when there is a possibility of favorable outcome with internal treatment, e g, in appendicitis without peritonitis, operation ought not to be carried out in a diabetic patient—J K

Transitory DIABETES after mumps (*Diabète transitoire post-ourlien*) Labbé (M) & Debré (R), *Bull et mém Soc méd des Hôp d Par*, 1921, 45, 1306-1309

A report of a case of hyperglycemia following pancreatic mumps —F S H

Practical treatment of DIABETES (*Die praktische Behandlung des Diabetes*) Lange (J), *München med Wchnschr*, 1921, 68, 1002

In the United States it seems, according to Lange, a not infrequent mistake to make a diagnosis of diabetes in cases of pentosuria. Pentosuria is not rare in America, which is due to the frequent use of fruit wines. Most doctors are too afraid of acetone. If a patient excretes 1-2 grams of acetone daily, even with diacetic acid, there is no danger of coma. Treatment consists mainly in avoiding over-eating, and reducing the large quantities of animal protein. A systematic treatment in a sanatorium should be recommended—J K

Syndrome of compression of the cavernous sinus accompanied by DIABETES INSIPIDUS and "basedowification" of a goiter (*Syndrome de compression de sinus caveux, avec diabète insipide et basedowification d'une goître*) Ledoux (E), *Bull et mém Soc méd d hôp de Par*, 1921, 45, 827-830

Presentation of a case as described in the title Polyuria was present, which yielded to the injection of posterior lobe extract The patient recovered from all his troubles spontaneously The disturbances are attributed to an enlargement of the posterior lobe of the hypophysis —F S H

DIABETES MELLITUS, syphilis, and the negro Lemann (I I),
Am J M Sc (Phila), 1921, 162, 226-230

This study is based on the experience of the Charity Hospital at New Orleans From 1898-1909, 61,298 admissions included 45 white and 19 negro diabetics Although the negroes furnished 40 per cent of admissions, they gave only 30 per cent of the diabetics From 1910-1919, inclusive, there were 160,044 admissions in which there were 135 white and 59 negro diabetics Here the negroes furnished 43 per cent of the admissions and only 30 per cent of the diabetics The negro furnished at the same time more than 50 per cent of all the syphilitic diseases So the author concludes there is no relation between the incidence of diabetes mellitus and syphilis Hence there is no probable etiologic relation between the two Further, there is an unexplained immunity in the negro race to the production of spirochetal pancreatitis just as there is an unexplained immunity of the race to the production of locomotor ataxia —J F

The treatment of DIABETES (Zur Therapie des Diabetes mellitus)
Lenné, Deutsche med Wchnschr (Berlin), 1921, 47, 867-868

According to the author, it is nowadays "fashionable" to give diabetics as little protein as possible He considers this in general a mistake and believes that many cases of acidosis and coma are due to low protein diet In coma administration of alkali never is successful When carbohydrate treatment is employed it is necessary to individualize There are patients who do better on a potato diet, while oatmeal gives no success In others the effect of oatmeal is splendid and potatoes have a bad influence Caramel, that has again been recommended in Germany, not only has a bad taste, but, though it does not increase glucosuria, fails likewise to decrease acidosis Cocoa and chocolate may be very useful Bitter chocolate containing little sugar often proves of much value in completing the diet —J K

Treatment of DIABETES (De praktijk der diabetesbehandeling)
Lubbers (H A), Nederl Tijdschr v Geneesk (Haarlem), 1921, 65 (II), 1841-1846

A general review of the treatment of diabetes With the Allen-Joslin method as well as with Falta's "Mehlfrüchtekur" good results may be obtained Individualization is necessary —J K

A study of **DIABETES INSIPIDUS** (Beitrag zur Lehre von Diabetes insipidus) Meyer (E) & Meyer-Bisch (E), Deutsch Arch f klin Med (Leipzig), 1921, **137**, 225-233

A girl of 18 who was very nervous suddenly developed polydipsia and polyuria. The average urine output was about 10 liters daily. Skiagrams of the skull showed no changes. When water was withheld for 6 hours the patient complained of palpitations and severe headache. The urine output during these 6 hours was 2080 cc. The NaCl concentration of the blood rose from 0.645% to 0.71%. The concentration of the urine rose from 0.04% to 0.12%. These facts prove the case to be one of real diabetes insipidus and, according to Veill (See Endocrinol, 1919, **3**, 195), a hyperchloremic case of this disease. The effect of pituitrin was very marked. It was injected for a period of 8 days, the NaCl content of the blood became 0.58%. The authors tried to find out whether pituitrin acts only upon the kidneys or also on the tissues. A canule was introduced into the ductus thoracicus of a dog and the lymph collected. Injection of pituglandol decreased the quantity of lymph, the protein and NaCl concentration were increased. After the injection the blood at first was slightly diluted, but later the concentration of hemoglobin, erythrocytes and serum protein became higher. These two facts prove that pituglandol increases the property of the tissues to retain water. Pituitrin thus has a double effect, one on the tissues and one on the kidneys —J K

(**DIABETES**) The ammonia content of the blood, and its bearing on the mechanism of acid neutralization in the animal organism Nash (T P) & Benedict (S R), J Biol Chem (Balt), 1921, **48**, 463-488

It would appear as if in diabetes there is an introduction into the blood stream of acid radicles more rapidly than the normal kidney can eliminate them, or can make ammonia to combine with them while eliminating them —F S H

Modern treatment of **DIABETES** (Ueber der jetzigen Stand der Diabetestherapie) v Noorden (C), München med Wchnschr, 1921, **68**, 1064

The underfeeding treatment must not be exaggerated. Though carbohydrate treatment is extremely useful, especially in cases with acidosis, the "Mehlfruchtekur" as described by Falta cannot be recommended, since this diet contains too small amounts of proteins. An intelligent diabetes diet must change from time to time. A diet rich in proteins and poor in carbohydrates, and another rich in carbohydrates and poor in proteins may be used alternatively —J K

Vegetable problems in **DIABETIC** diets Orton (W A), Am J M Sc (Phila), 1921, **162**, 498-509

A most interesting discussion by an agriculturist of the food supply of the diabetic. A list of vegetables for a "diabetic garden" is given. The author grew this year 81 species in 255 varieties and has accomplished the aim of having some fresh green vegetables of his own growing every day in the year without a greenhouse —J F

Ear complications in DIABETES (*Complicazioni otitiche in diabetes*)
Perrone (P), Il Morgagni (Milano), 1921, 64, 178-196

Report of the complications of purulent otitis media, and meningitis purulenta in diabetes. The author concludes that it is not justifiable to wait till all symptoms are present, but the operation should be performed as soon as possible. If, however, it is possible two or three weeks before the operation, anti-diabetic treatment should be instituted, this will largely diminish the risks of the operation. The operation should be carried out under light ether narcosis or under local anaesthesia. The operating should be done as quickly and simply as possible. Both the mastoid and dura mater should receive due attention in the operation —J K

DIABETIC coma and convulsive crises *Acidosis and meningeal hemorrhage* (*Coma diabétique et crises convulsives* *Acidose et hémorragie méningée*) Rathery (F), Cambessedès & Welti, Bull et mém soc méd des hôp de Par, 1921, 45, 1265-1268

Report of a case as described in the title —F S H

Urine in DIABETES MELLITUS Richards (J H), N York State J M, 1918, 18, 193

There may be an increased excretion of NH_3 in the absence of urinary acetone bodies, and a normal excretion of NH_3 in their presence. The quantity of sugar excretion has no relation to the N distribution of the urine. In many cases there is a N disturbance which may be corrected by regulating the N intake, but no correction of urinary nor acetone bodies will correct this N disturbance —Physiol Abst, 3, 434

Researches on DIABETES (*Beiträge zur Diabetesforschung* I, II, III, IV) Sakaguchi (K), Mitt a d Fakult d k Univ zu Tokyo, 1918, 20, 345-373, 439

Sakaguchi reports an exhaustive study of various features of diabetes. He discusses why the tolerance of diabetics is the lowest at breakfast and the elimination of sugar the highest after this meal. His conclusion is that this is due to the fact that the production of glycogen is less after breakfast than at other meals. The elimination of sugar after breakfast can be reduced by giving a little carbohydrate or meat an hour or two before the breakfast. He states further that carbohydrates to the limit of tolerance are borne better

if taken four or five hours after the preceding meal. When the interval is six hours or more, the glycosuria may be increased. Clinical evidence is presented to show the injurious action of emotional stress on the sugar content of the blood, while brain work, without emotional disturbance, does not modify the glycemia. In the three cases described, the sugar content of the blood was determined before and after the patients had been informed of the serious nature of their disease. Diabetics should avoid occupations, he suggests, that entail worry or excitement. The fourth communication discusses the influence of intake of albumin on the sugar content of the blood. As the considerable rise in the sugar content reaches its highest point in from two to four hours after eating meat, it seems to be due to the products of digestion in the small intestine, rather than to the products of putrefaction of albumin in the large intestine.

—J Am M Ass

(DIABETES) Cholesterin in blood serum (*Ueber den Cholesteringehalt des Blutserum bei Krankheiten*) Stepp (W), München med Wchnschr, 1918, 65, 781-785

A increase occurs in diabetes, certain liver diseases and nephritis—Physiol Abst, 3, 576

(DIABETES) Critical analytical discussion and experiments in the determination of the blood sugar in health and disease (*Kritisch analytische Betrachtungen und Untersuchungen zur Bestimmung des wahren Blutzuckers bei Gesunden und Kranken*) Stepp (W), Arch f exp Path u Pharm (Leipzig), 1921, 90, 105-128

In estimating the amount of blood sugar it is necessary, when working with a reduction method, to remove not only the proteins but also other substances with reducing properties such as uric acid, creatinin, and amino acids from the serum. Mixing the serum with phosphotungstic acid is a better method than the use of colloidal iron oxide. When the blood sugar is estimated after precipitation with phosphotungstic acid and evaporation the amount of reducing substances is diminished. The best way to determine the blood sugar is by polarization or fermentation. The results of the reducing methods are 40 to 100 per cent too high—J K

DIABETES INSIPIDUS Umber, Deutsche med Wchnschr (Berlin), 1921, 47, 763

A demonstration of a patient with polyuria, headaches, hemianopsia. No change in the sella turcica was found. The Wassermann reaction was strongly positive. Antisyphilitic treatment gave good results, and the eye symptoms disappeared completely—J K

The retinitis of DIABETES MELLITUS Wagner (H P) & Wilder (R M), Collected Papers of Mayo Clinic, 1920, 12, 756-761
(Reprint from J Am M Ass, 76, 515-517)

From an intensive study of the cases of diabetes at the Mayo Clinic the authors conclude that the primary cause of the retinitis of diabetes lies in the accompanying pathologic changes in the vascular system —J F

Plasma chlorides and edema in DIABETES MELLITUS Wilder (R M) & Beeler (Carol), Collected Papers of Mayo Clinic, 1920, 12, 398-405

Data are presented to show that edema in diabetes differs fundamentally from the edemas in diseases of the heart and kidneys The determining factor seems to be inanition, which relates it to the hunger edema of war times and the other edematous condition of undernutrition —J F

(DIABETES MELLITUS) An evaluation of the Allen method of treatment Williams (J R), Am J M Sc (Phila), 1921, 102, 62-72

A report of the application of this method to 103 cases treated in the author's clinic since 1915 He concludes that the Allen treatment is a distinct clinical advance In the majority of cases its value is in inverse proportion to the seriousness of the failure of metabolism The treatment is of little avail when serious infections are present or when the patient is afflicted with the degenerative processes of old age Many patients find the treatment too exacting A very considerable proportion of those who die from diabetes are patients with severe cases who willfully violate their diets and rapidly succumb Fewer than 14 per cent were persistently faithful to the treatment Many die because of lack of courage Patients with serious or hopeless complications frequently abandon dietary treatment Often in adults death resulted because of the inability of the patients to provide suitable care Neglected diabetes is more rapidly and certainly fatal in a child than in an adult The majority of patients who live within their food tolerance gain in physical vigor, furthermore, the distressing symptoms incident to the disease noticeably lessen Moderately severe cases do surprisingly well Severe cases which have not been rigidly dieted are markedly benefited by the institution of the Allen treatment Patients who have been dieted carefully for long periods do less well Kidney functional tests in thirty-nine cases after the administration of thirty doses of arsphenamin, each dose consisting of 4.6 g and distributed over a two-year period failed to give any conclusive evidence of injury to the kidneys —J F

Examination of the blood in DIABETES mellitus Williamson (R T), Practitioner (London), 1921, 107, 169-173

The author describes his method for estimating the sugar content of the blood, originally published in 1896. It is useful in detecting marked increase above normal blood sugar value, but is not available for estimating slight changes. Only one large drop of blood is required. This is an advantage, and the procedure is so simple that it may be performed at the bedside. The author himself remarks that other blood tests are necessary and desirable for indicating the exact percentage of sugar.—H L

The relation of the DUCTLESS GLANDS to gynecology physiological and therapeutic Bigelow (Alice H), Boston M & S J, 1918, 178, 715-718

A classification of the endocrine glands is given on the basis of those which accelerate and those which retard metabolic processes. The former group includes the thyroid, ovaries, testicles, posterior lobe of the pituitary, and the medulla of the adrenal. The opposite group embraces the parathyroid, anterior lobe of the pituitary, suprarenal cortex and probably thymus and pineal. Among the gynecological applications of endocrine knowledge and therapy briefly discussed are the atrophy of the thymus at puberty, the exaggeration of secondary sex markings with acromegaly, and the genital retrogression of hypopituitarism, the amenorrhea often seen with thyroid disorders and with pituitary insufficiency. The article concludes with a short discussion of ovarian therapy in such conditions as the above.—E N

(ENDOCRINE) On fits, epileptic and others Feiling (A), Practitioner (London), 1921, 107, 22-32

The author presents a classification of "epileptiform fits" according to etiology and it is interesting to note that no mention of so-called pituitary or ovarian epilepsy is therein made. However, toward the end of the article the following sentence occurs: "The frequent association in women of epileptic fits with menstrual periods raises the question whether some biochemical or endocrine factor may be the cause"—H L

The relation of eclampsia to the ENDOCRINE ORGANS of the child (Die Beziehung der Eklampsie zum endokrinen Drusensystem des Kindes) Fraenkel (M), Zentralbl f Gyn (Leipzig), 1921, 45, 929-930

Many years ago the author described a case of eclampsia in the 7th month of pregnancy. At post-mortem the child showed a large thyroid and a small thymus. He now reports two similar cases (no details are given) and believes that the endocrine system of the mother takes the place of the endocrine system of the child. The primary cause of eclampsia is probably, in his opinion, endocrine

insufficiency of the child (As no clinical details are given it is difficult to decide whether this little article is as full of nonsense as it appears)—J K

(ENDOCRINE) The ductless glands and constitutional diagnosis Gutman (J), Med Woman's J (Cincin), 1920, 27, 281-286

See Endocrin , 4, 624

(ENDOCRINE GLANDS) Glandular dystrophies and particularly mono-symptomatic dystrophies (Dystrophies glandulaires et particulièrement dystrophies mono-symptomatiques) Hutinel (V) & Maillet (M), Ann de méd (Paris), 1921, 10, 89-114

A lengthy discussion in which total dystrophies or endocrine cachexias, such as myxedema, cretinism, cachexia strumipriva and pachydermal cachexia are considered together with adrenal and hypophyseal dysfunctions General systematized dystrophies are considered as in a class by themselves, examples of which are various hyper- and hypo-thyroid states, acromegaly, gigantism, nanism, the adiposo-genital syndrome, adrenal pseudo-hermaphroditism, adrenal virilism and hirsutism In fact, the whole range of disorders rightly or wrongly attributed to disturbances of function of single endocrine glands is succinctly reviewed in a masterly fashion—F S H

Pathology of the ENDOCRINE organs (Zur Pathologie der Endokrinen Drusen) Lohlein, München med Wchnschr, 1921, 68, 1036

A short note In a case of osteitis fibrosa an adenoma of one parathyroid was found In a boy of 15 with infantile testicles and absence of secondary sexual characters with a slight degree of adiposity a teratoma of the pineal was found The author believes this to be a case of dystrophia adiposo-genitalis from hydrocephalus with pressure on the pars posterior of the hypophysis—J K

(ENDOCRINE ORGANS) Osteomalacia and hereditary lues (Osteomalacia y heredo-lues) Malamud (Teresa), Prensa Méd Argent (Buenos Aires), 1921, 7, 264

Report of a case diagnosed as osteomalacia, which was attributed to hereditary syphilis producing a pluriglandular syndrome —B A H

New questions on the ENDOCRINE GLANDS (Neue Fragestellungen in der Lehre von der inneren Sekretion) Münzer, Fortschr d Med (Berlin), 1921, 39, 765-767

The "new" observations of Münzer are rather old He states that endocrine diseases are nearly always polyglandular He believes that it is possible to express polyglandular diseases by mathematical

formulas e g , **Acromegaly**=**Hyperfunction** of **hypophysis** plus **hyper-** or **hypo-** (') **function** of **thyroid** plus **hyperfunction** of **adrenals** plus **hypofunction** of **gonads** plus **hyperfunction** of **thymus** (?) It is not necessary that a disease begin in the gland that is the chief etiologic factor of this disease **Acromegaly** can perhaps just as well begin with a **hypofunction** of the **testicle** as with **hyperfunction** of the **hypophysis** (The abstractor ventures to hope that this algebraic endocrinology will not be the beginning of a new series of nonsensical pronouncements on the physiology of the endocrine organs)—J K

ENDOCRINE disturbance in mental defectives Murdock (J M), Penn M J (Harrisburg), 1921, 25, 50

The author reports that a considerable proportion of mental defectives show evidence of internal secretory disorders, mostly **hypothyroidism** or **hypopituitarism** The mental defect is not necessarily the result of the glandular dysfunction, both may be due to an underlying cause These changes frequently originate early in childhood A plea is made for early recognition so that appropriate therapy may be instituted at a time when improvement is possible After definite somatic changes have taken place, treatment is more difficult and less promising In 100 autopsies of feeble minded patients reported by Raeder of the Massachusetts State Psychiatric Institute, 76% showed endocrine anomalies —H L

ENDOCRINOLOGY Noyons (A K), Vlaamsch Geneesk Tijdschr (Ghent), 1921, 2, 385-392

A general review, without new facts Some statements are rather doubtful The "adrenal" is called the perfect type of an endocrine gland It is stated that removal of the adrenals in an animal is not an important operation —J K

Modifications in the ENDOCRINE GLANDS and in the blood of the chicken following the injection of adrenalin and of cholin (Modificazioni nelle glandole endocrine e nel sangue dei polli iniettati con adrenalina e colina) Pighini (G), Biochim e Terap Sperim (Milano), 1921, 8, 140-154

The chickens experimented upon were between 2½ and 18 months of age The adrenalin (1 1000) was used hypodermatically, endomuscularly and sometimes intravenously in doses of 1 cc The cholin used was the hydrochlorate (Meck) 1 per cent in doses of ½-1 cc, either hypodermatically or intravenously Besides the behavior of the blood, the following organs were studied **brain**, **hypophysis**, **thyroid**, **liver**, **spleen**, **pancreas**, **adrenal glands**, **kidney**, **testis**, **ovary** As regards adrenalin, the younger subjects offered less resistance, but all showed a great deal of adaptation to the drug, after

the first doses, as shown by their behavior and by autopsy findings. The organs, which showed a constant, well accentuated reaction, were thymus, spleen, adrenal glands and blood. Interesting effects of cholin on thyroid were also seen. As an effect of adrenalin parenchymal degeneration of the thymus occurred characterized by extreme reduction of the lymphatic elements of the cortex, of the corpuscles of Hassall and lipoid degeneration of the epithelial elements. An accentuated reduction of the Malpighian elements in the spleen and hypertrophy of the chromophil tissue in the adrenal glands, accompanied by diminution of lipoids in the cortex, were seen. The blood showed a neutrophilic leukocytosis. The effects of cholin on the thymus were increased function and hypertrophic characteristics of the medulla, increased number of Hassall's corpuscles, numerous forms of hypertrophied epithelioid cells—myoid and giant—and colloidal cysts. In the thyroid hyperplastic changes were noted. Hypertrophy of the Malpighian corpuscles and tendency to hypertrophy of the interrenal tissue was seen in the spleen and in the blood, slight polynucleocytosis. The author insists that, while the thymus is always found hypertrophied and hyperactive after cholin administration, the thyroid appears hyperplastic. These two changes do not seem accidental, but might be referred to the relations between thyroid and thymus postulated in Basedow's disease. The data are taken to indicate a decided antagonism between adrenalin and cholin. This is being further studied.—G V

The relation of ENDOCRINOLOGY to vegetative or visceral neurology Pottenger, (F M), N York M J (New York), 1921, 113, 364-366

All smooth muscle and all secreting glands are innervated by vegetative nerves and activated by the products of the glands of internal secretion. The internal secretions act through or with one or the other division of the vegetative system, either as a whole or in some part of its distribution, hence vegetative functions, whether controlled through nerves or through internal secretions, can be divided into those which depend upon the sympathetic and those which depend upon the parasympathetic nerves for their activity. The sympathetics have for their function the defense of the body, while the parasympathetic system controls the intake and digestion of food. Disease interferes with the normal functions of defense and self-preservation, i e., sympathetic and parasympathetic functioning. The individual will be able to execute these two outstanding purposes upon which his life depends in accordance with the stability or instability of his vegetative nervous and endocrine systems.—H W

The relation of the ENDOCRINE system to the glycemic reaction following the injection of homologous protein Rohdenburg (G L) & Krehbiel (O), Am J M Sc (Phila), 1921, 162, 28-40

The authors report the effect of ablation of one or more glands of internal secretion upon the glyceimic reaction. Albino rats were used. Blood sugar determinations were made by the method of Epstein. In a series of seventy normal, fully grown, healthy rats the blood sugar values were determined before and after injection of homologous protein. A variation between the preinjection sample and that taken 60 minutes after injection of 16 or more mgm was taken as a positive reaction. In this series it was found that 73 per cent gave a positive reaction and that the average difference was 29 mgm. In the first experiments, a single "internal secretory" gland was removed. The glands entirely removed individually were the spleen, thymus, both testes, both ovaries, both adrenals, approximately 90 per cent of the thyroid and embedded parathyroids, and approximately 90 per cent of the pancreas. There were six animals in each group. In the second experiments, double ablations were performed in such rotation that all possible combinations were obtained, for example, testes-spleen, testes-thyroid, testes-adrenal, testes-pancreas. In each of these groups there were also six animals. There were two combinations of organs which, when ablated, inhibit the glyceimic reaction, (1) spleen and either gonad set, (2) adrenal and pancreas. If one gland from either system be ablated and with it one gland from the other system, there results little or no change from the normal reaction. If, however, one gland from one system be removed with one gland from the other system, and, in addition, either the thyroid or thymus, then marked inhibition occurs. Removal of one gland from one system and of either the thyroid or the thymus results in practically no inhibition. If both glands be removed from each system, then, in order to induce inhibition, both of the intermediate glands must also be removed. From this it would appear that there are two systems which control the reaction and that these systems are connected through two apparently interchangeable glands, the thyroid and the thymus.—J F

ENDOCRINE organs in experimental gas gangrene (*Les organes a sécrétion interne dans la gangrène gazeuse expérimentale*) Van Geheuchten (P), *Ann de l'inst Pasteur (Paris)*, 1921, 35, 396-419

After giving a comprehensive review of the literature dealing with the effect of gas gangrene on the endocrine organs the author proceeds to describe the results of his own experiments on 65 guinea pigs treated with various types of gas producing bacilli. The results of his study indicate that the modifications of the glands of internal secretion in the infections caused by the anerobic micro-organisms are entirely comparable to those observed in infections and intoxications of very diverse origin. They are of slight degree in the thyroid and the hypophysis and severe in the adrenal capsule margins. In the latter the lesions are characterized by a discharge of the lipid

material of the spongiosa into the blood, and almost all the cholesterol is lost within about 48 hours. The neutral fats disappear somewhat less rapidly. They persist and even increase in the glomerulae and neighboring cells—F S H

Case of GIGANTISM (Geval van reuzengroei) Hekman (J J), *Nederl Tijdschr v Geneesk* (Haarlem), 1921, 65 (II), 1498

Demonstration of a tall girl of 19 (190 cm). Hands, arms, feet and legs were very long. There were axillary and pubic hairs. Menstruation began at 17 and has been normal. No changes in the sella or in the eyes were noted. The bone formation was retarded as shown by radioscopy. There was a slight prognathism. Blood sugar on the empty stomach was 0.14%, after 100 gm glucose was 0.24%. The most probable diagnosis is dysfunction of the hypophysis with a secondary insufficiency of the ovaries—J K

(GONADS) A case of hermaphroditism (Ein Fall von Hermaphroditismus) Beneke, *München med Wchnschr*, 1921, 68, 1064

Under the long clitoris ended a hypospadias urethra, which led to the vagina and the small uterus. Instead of the ovaries there was on the right side a very small organ with a few paradidymis canals and on the left side an organ the size of a pea with small seminal canals—J K

(GONADS) Steinach's theory of a puberty-gland (Zur Lehre Steinachs von der Pubertätsdrüse) Dietrich (A), *Deutsche med Wchnschr*, (Berlin), 1921, 47, 1080, *München med Wchnschr*, 1921, 68, 1034-1035

The interstitial cells of the testicles have a nutritive role, they play an important part in the resorption of substances formed in the other cells. Neither in the testicle or ovary has an independent function of the interstitial cells been proved—J K

(GONADS) Steinach's operation (Die Steinachsche Methode) Klein, *Berlin klin Wchnschr*, 1921, 58, 1087, *Wiener klin Wchnschr*, 1921, 34, 518

Indications for the transplantation of testicles are deficiency symptoms after castration, eunuchoidism, and homosexuality. In this last case a testicle must first be removed. Testicles of animals are perhaps useful. For the ligation of the vas deferens precocious senility is the most important indication. In cases of hyperfunction of one testicle, ligation of the corresponding vas deferens is perhaps useful—J K

(GONADS) Carbohydrate content of the King salmon tissues during the spawning migration Greene (C W), *J Biol Chem* (Balt), 1921, 48, 429-436

The ovaries of the series of 6 fish are remarkably uniform in glucose content whatever the stages of the journey to spawning. The percentages are from 0.08 to 0.18. The analysis of one lot of eggs free from ovarian tissue gave 0.09% glucose. This is near the average for the ovary of the series of immature fish. It demonstrates that the carbohydrate content in this growing tissue is independent of the stage of development and the duration of the fast. No glucose was found in the testes of nearly mature salmon.

—F S H

Function of the GONADS and psychical disturbances (*Keimdrüsenfunktion und Seelenstörung*) Kretschmer (E), *Deutsche med Wchnschr* (Berlin), 1921, 47, 649-650

The author points out the importance of the endocrine functions of the sexual glands in psychical diseases as is proven by the sexual symptoms of patients with such disturbances and the psychical symptoms as seen in diseases of the sexual organs.—J K.

(GONADS) Steinach's operation in sexual impotency (*Steinachsche Operation in der Behandlung der Impotenz*) Littaur, *Deutsche med Wchnschr* (Berlin), 1921, 47, 1248

Littaur has seen good effects from this treatment. The only proof that is given is that—the patients wrote him very grateful letters!—J K.

(GONADS) A criticism of Steinach's rejuvenation operation (*Zur Beurteilung der Steinachschen Verjüngungsoperation*) Mendel (K), *Deutsche med Wchnschr* (Berlin), 1921, 47, 986-989

A healthy man with precocious senility was operated upon by ligation of the vas deferens. Immediately after the operation a psychosis developed with serious sexual irritability and sexual hallucinations. Death followed. The author warns against this treatment. It has not been proved that Steinach's "Pubertätsdrüse" exists. It has not been proved that ligation of the vas deferens between the epididymis and testis causes a rejuvenation of the interstitial cells. Experiments on rats cannot be compared to clinical work in man. Steinach's operation is not without danger as is proved by the case cited. Transplantation of testicles may be considered as at least a more logical operation than ligation of the vas deferens.—J K.

(GONADS) Steinach's rejuvenation operation (*Die Steinachsche Verjüngungsoperation*) Mendel (K), *Berl klin Wchnschr*, 1921, 58, 1011

Data have been reported in the *Deutsche med Wchnschr*—J K.

A chemical fact in the study of the GONADS (*Contributi chimici allo studio delle ghiandole genitali*) Russo (G), Gazz d Osp (Milano), 1921, 42, 735

In some animals the testicles contain much more nitrogen when active than when at rest In the ovaries this difference is much smaller —J K

(GONADS) Clinical influence of ligation of the vas deferens (*Die klinische Wirkungen der Vasoligatur*) Schmidt (P), Deutsche med Wchnschr (Berlin), 1921, 47, 1248

The author has carried out Steinach's operation in 20 cases The effect on the sexual disturbances is splendid (As no details are given, it is impossible to evaluate this statement) —J K

(GONADS) Formation of a hymen in the urethra (*Ueber Hymenbildung in der Harnrohre*) Schmincke, Berlin klin Wchnschr, 1921, 58, 1020

A man of 22 died of a sarcoma of the neck At the autopsy there was found cryptorchism, with absence of beard and pubic hair In the pars prostatica of the urethra was a hymen which closed the entrance of the vagina masculina The diagnosis was pseudo-hermaphroditismus masculinus internus —J K

HYPERNEPHROMA Gagstetter, Deutsche med Wchnschr (Berlin), 1921, 47, 1150

Of no endocrine interest —J K

HYPERTENSION (*Kurzen Beitrag zur Frage der Hypertonie*) Fahr (T), Berl klin Wchnschr, 1921, 58, 730-731

Most authors believe that in arteriosclerotic hypertension the sclerosis of the blood vessels is caused by the high blood-pressure Fahr, however, has always believed that sclerosis (especially of the vessels of the kidney) occurs first, and later, a rise of blood pressure In 1910 Neubauer stated that in hypertension there is always hyperglycemia Many authors did not find this, but now Neubauer's views have been entirely confirmed by Hitzenberg and Richter Quittner (*Wiener Arch f inn Med*, 1921, 2, 189) These authors believe that there is an increase of *adrenalin* in the blood and that this causes both the increased blood sugar and the rise of the blood pressure Fahr states that the increased amount of blood sugar may be due to a primary sclerosis of the vessels of the pancreas It is well known that the vessels of this organ often show arteriosclerotic changes He believes that this is followed by the secretion of a diminished quantity of hormone and that this causes the hyperglycemia On the other hand, there is an antagonism between the pancreas and chromophil tissue Thus the high blood pressure as

well as the hyperglycemia may also be due partly to an increased secretion of adrenalin (The article is full of unproved statements)

—J K

(HYPOPHYSIS) Hypopituitarism after cerebral influenza (Hypopituitarismus nach Gehirn-Grippe) Fendel, Deutsche med Wchnschr (Berlin), 1921, 47, 991

A boy of 13 became very fat following an attack of influenza. A skiagram of the sella turcica was not made. There was no genital atrophy, no symptoms of brain tumor nor hemianopsia. The intelligence was normal. (The abstractor is not able to understand why this is regarded as a case of hypopituitarism) —J K

Diagnosis of HYPOPHYSIS insufficiency (Diagnose van der hypophysenzwakte) Fliess (W), Med Weekblad (Haarlem), 1921, 28, 309-315

A translation of an article from the Med Klinik —J K

(HYPOPHYSIS) A case of acromegalic giantism (Sobre um caso de gigantismo acromegalico) Flores (N) & Diaz (A), Revista dos Cursos (Porto Alegre), 1921, 7, 159-174

The case is that of a typical acromegalic giant 2 16 m tall with a reach of 2 31 m. He was only slightly active sexually, and had moderately developed external genitalia. There was a slight degree of kyphosis. There was no glycosuria, glycemia was 0 136, acidity of urine was 0 00052, creatinin, 0 0013, blood cholesterin, 0 633. There was chronic choked disc of the right eye. The sella turcica was enlarged —B A H

The PITUITARY gland in children Fraser (J), Edinb M J, 1921, 27, 136-144

This study is based upon a series of forty pituitary glands obtained from children between the ages of one year and twelve years. Comparing the pituitary of the child with that of the adult it is found that the variation in the size of the "pituitary lake" (intra-glandular cleft, Koelliker's space, the remains of the original cavity of Rathke's pouch) is apparently a feature distinctive to the child, or at least to the period between birth and adolescence. The author holds that in children the pituitary exhibits distinct periods of activity and rest. There seems to be a distinct relation between the stage of activity of the pars intermedia and the amount of distention of the pituitary lake. While the pars intermedia is in a resting state the lake is small, and in certain cases practically empty. As the pars intermedia becomes more active, secretion begins to accumulate within the lake until it becomes distended to a considerable degree. The pars intermedia then returns to its resting state,

and the lake gradually returns to a slit-like space. The author believes that the major part of the contents of the lake is a homogeneous colloid material derived from the pars intermedia, there is also a secondary contribution from the eosinophil cells of the anterior lobe. There is found to be an active stage of the anterior lobe which is synchronous with the active stage of the pars intermedia, and is partly preliminary and partly synchronous with the distention of the pituitary lake. The changes of stage noted are the same in the two sexes. They have no relationship to any morbid condition.—W J A

(THYROID) Suggestions regarding the role of the **HYPOPHYSIS** in Graves' disease and myxedema. Friedman (G A), N York M J (New York), 1921, 113, 370-374

The hypophysis appears to show histological changes in Graves' disease similar to those of hyperpituitarism and in myxedema to those of hypopituitarism. Therefore, there is a certain degree of hypophyseal involvement in conditions of disturbed thyroid function. Chromophilia of the anterior lobe is characteristic for Graves' disease, chromophobia for myxedema. The following symptoms and signs of Graves' disease may in part be attributed to hypophyseal overactivity: increased metabolic rate (emaciation), tendency to glycosuria, insomnia and irritability, intestinal spasticity, tendency to miscarriage, and acceleration of epiphyseal closure. The symptoms and signs of myxedema attributable to hypophyseal underactivity are as follows: decreased metabolic rate (adiposity), high sugar tolerance, mental depression, intestinal atony, rarity of miscarriage, and retardation of epiphyseal closure. Pituitary products should be contraindicated in the treatment of exophthalmic goiter patients and indicated in addition to thyroid in myxedematous subjects.—H W

(HYPOPHYSIS) Adiposogenital syndrome in adults (Contribution à l'étude du syndrome adipo-génital d'origine hypophysaire chez l'adulte). Goudal (J M), Thèse de Paris, 1919, 72 p, No 250

According to Goudal the adiposogenital syndrome in the adult is characterized by (1) rapid and progressive obesity, (2) atrophy of the genital organs and disappearance of the sexual functions, constituting late infantilism, (3) association of cerebral and visual disturbances. This triad of symptoms is sometimes accompanied by slight signs of acromegaly and frequently by diabetes insipidus. The diagnosis of the condition rests on the presence of the ocular signs, especially bitemporal hemianopsia, so that the patients are frequently sent to the physician by the oculist who finds other signs of the syndrome present.—Med Sc Abst & Rev, 1920, 2, 134

(HYPOPHYSIS) Defects of membranous bones, exophthalmos and polyuria in childhood Is it dyspituitarism? Hand (A), Am J M Sc (Phila), 1921, 162, 509-515

The author has in times past reported cases of children presenting this triad of symptoms as associated with tuberculosis He brings forward his own cases again and discusses them in the light of similar studies by others together with a new case and the review of theories which have been advanced He concludes that further data are needed for a satisfactory explanation —J F

(HYPOPHYSIS) Dyspituitarism so-called absorption of membranous bones, exophthalmos and polyuria. Report of two cases Hand (A), Tr Am Pediat Soc , 1920, 32, 154

Hand reviews the literature on this peculiar condition Six cases have been reported by Christian, Schiller (2), Kay, and himself He goes into detail in his own cases A boy three years of age had had great thirst and polyuria for 8 weeks He was undersized, and had bronzed skin There was exophthalmos The thyroid was not enlarged There was abdominal distention with an enlarged liver and spleen and umbilical hernia The skin over the abdomen presented eczema and petechial eruption The urine was sugar-free, but showed some albumin He ran an irregular temperature from 99° to 105°, which reacted somewhat to quinine Broncho-pneumonia set in later, but a diagnosis of tuberculosis was made because of the general course of the disease The boy died suddenly At the post-mortem examination, as the scalp was stripped off, a yellow spot about 2 cm in diameter was noticed extending through the entire thickness of the skull, it was soft and movable Other small areas which did not extend through the vault were seen on the outer surface These were thought to be tubercular

The second was a boy of four years At the age of two, a tumor-like mass had been removed from the left parietal region There was an absence of bone beneath it down to the dura There was no evidence of its being a gumma or a sarcoma There was a slight degree of inflammation, mainly myxedematous Since then exophthalmos had developed, but no polyuria The radiogram of the skull showed bone changes, but no changes in the sella

Hand objects to the theory of hypopituitary etiology on the following grounds Two of the six reported cases have not shown polyuria In two having polyuria and probably in all four, exophthalmos and bone changes came first Injection of pituitary extract, although diminishing the polyuria, had no effect on the bone changes The exophthalmos is probably not of toxic or endocrinic origin, but mechanical, due to involvement of the orbital plate of the frontal bone as shown by the four who have been studied by the x-ray The bone changes are not such as would be produced by

a chemical substance, which ought to effect the bones in their entirety Polyuria probably depends upon disturbed function of the hypophysis, due to pressure Other possible theories are that the bone changes are those of osteosarcoma A chronic infective process may also be considered, since two of the cases started with decay of the teeth and two had a history of a discharging ear —M B G

The importance of HYPOPHYSEAL lesions in diabetes insipidus
(Über die Bedeutung der Hypophysenveränderungen bei Diabetes insipidus) v Hann (F), Frankf Ztschr f Path (Weisb), 1918, 21, 337-336

V Hann reports three cases with autopsy findings and reviews the literature of seventeen other cases with post-mortem findings He concludes that every case is associated with a "dysfunction" of the hypophysis Hypophyseal lesions are found in diabetes insipidus only when for some cause, as a tumor or inflammatory reaction, the posterior lobe is destroyed or severely injured while the anterior lobe remains functionally intact The onset of diabetes insipidus is dependent upon a functionally intact heart and renal system in addition to the functional disturbance of the neurohypophysis He found no evidence of associated thyroid disease in the cases reported —D M

Experiences with the extract of HYPOPHYSIS in labour (Unsere Erfahrungen mit dem Hypophysen-extrakt Physormon als Wehenmittel) Hellmuth (K), Centralbl f Gyn (Leipzig), 1921, 45, 1320-1324

This preparation is warmly recommended for obstetrical purposes It is an alcohol-chloroform extract from fresh hypophyses (pars posterior and intermedia) of cows —J K

Action of HYPOPHYSIS extract in cerebral polyuria (Acción del extracto de hipofisis sobre la poliuria cerebral) Houssay (B A) & Hug (E), Rev Asoc méd argent (Buenos Aires), 1921, 34, 443

It is necessary to distinguish the immediate action and that over a period of 24 hours in studying hypophysis extract In the normal dog or in one having polyuria there is always an immediate increase in diuresis Polyuria was produced by ablation of the hypophysis or by piqure in the para-infundibular region —B A H

Tumor of HYPOPHYSIS successfully removed (Glücklich operierter Hypophysentumor) Kirschner, Deutsche med Wchnschr (Berlin, 1921, 47, 879-880 (Berl klin Wchnschr, 1921, 58, 976-977)

The patient had diminution of the visual field and decreased vision The endonasal removal of an angiosarcoma of the hypophy-

sis was followed by marked improvement The visual field became nearly normal again —J K

Assay of HYPOPHYSEAL preparations and other materials used in labor (Zur Wertbestimmung der Hypophysenpräparate und anderer Wehenmittel) Kochmann (M), Ztschr f physiol Chem (Berl u Leipz), 1921, 115, 305-310

This method based on the contraction of the uterine segment does not differ in any essential particular from those already found in the literature with the possible exception that the rhythmical contractions of the uterus are inhibited by suspending the segment in a Ca-poor Ringer's solution to which MgCl₂ has been added

—F S H

The opinion of the clinic in Utrecht about the use of PITUITRIN (Het standpunt der Utrechtsche Kliniek ten opzichte van het gebruik van pituitrine) Kouwer (B J), Vox Medicorum (Utrecht), 1921, 21, 129-131

The author is the director of the University Clinic for obstetrics in Utrecht The first essential in obstetrical practice, he believes, is patience He thinks that if students are taught to use pituitrin they will abuse it when they enter practice It is not easy to give a satisfactory indication for the use of pituitrin In 20,000 child-births the author reports that pituitrin was given 15 or 20 times In many of these cases the injections produced no results —J K

(HYPOPHYSIS) Report on the regulation of the use of bichloride of mercury and pituitrin by mid-wives (Rapport sur la réglementation de l'emploi par les sages femmes du sublimé et de la pituitrine) Le Lorier, Bull soc obst et gyn d Par , 1921, 10, 312-320

Hypophyseal preparations of any type should be considered as dangerous drugs and their use should be forbidden to mid-wives

—F S H

Diabète insipide et HYPOPHYSE Lereboullet (P), Progress méd (Par), 1919, 3 s 34, 363-366

Lereboullet in the course of his regular lecture on this subject describes the case of a man of 50 who had had syphilis at 18 and at 31 protracted pneumonia, after which there was retrogressive infantilism, impotence, asthenia, falling of the hair and tendency to obesity There was also polyuria Treatment of various kinds proved futile until pituitary treatment was given, and then the output of urine dropped from the 7 or 8 liters, which had been the average for ten years, to the normal figure as long as the pituitary

treatment was kept up The extract from the posterior lobe alone was most effectual—J Am M Ass, 73, 1731

Opothérapie HYPOPHYSAIRE et diabete insipide Lereboullet (P), Paris méd, 1919, 9, 353-357

Lereboullet alludes to a case of diabetes insipidus reported by him five years ago in which the symptoms were temporarily relieved by subcutaneous injection of the posterior lobe of the hypophysis Since then many other similar cases have been published showing that diabetes insipidus is often the direct or indirect manifestation of a change in the hypophysis which can be benefited by such treatment Its action, however, is only transitory and rarely lasts more than twenty-four hours The treatment therefore does not modify to any extent the prognosis of diabetes insipidus It cannot remove the causal lesion or render etiological treatment unnecessary, e g, when the condition is due to inherited or acquired syphilis It does not prevent a subsequent operation which is always serious and often fatal But its value lies in causing a temporary relief of the patient's symptoms It dispels the intense thirst for a few hours, calms the nervous symptoms, and restores sleep The treatment is quite harmless, so that daily injections of 1-2 cc of the extract of the posterior lobe may be continued for a long period, and will be found to have a favorable action not only on the diuresis and thirst, but also on the obesity, general condition, development of the genital system, and even on growth—Med Sc Abst & Rev

(HYPOPHYSIS) Action vasculaire comparée de l'histamine et de l'extrait d'hypophyse associées à l'adrénaline Llosa (J B), Compt rend Soc de biol (Par), 1920, 83, 1358

See Endocrin, 5, 362

The question of PITUITRIN (Het pituitrinevraagstuk) Mendels (W A), Vox Medicorum (Utrecht), 1921, 21, 154-155

Mendels states that in 1,000 injections of pituitrin in child-birth he has never observed any undesirable results It is a valuable drug, especially in multiparae As even the smallest trace of alcohol destroys the activity of pituitrin, the syringe should not be cleaned with it He recommends an American preparation, and mentions several German and Dutch preparations of pituitrin as inactive and useless [The opinion that alcohol injures pituitrin has not been sustained by careful American investigation—Ed]—J K

Extirpation of HYPOPHYSIS Oehlecker, Berlin klin Wehnschr, 1921, 58, 821

In case of a patient with acromegaly and another with dystrophia adiposogenitalis, Oehlecker removed the hypophysis by a

modification of Schloffer's operation with good result In 3 other cases in which other tumors pressed on the hypophysis the operation failed to prevent a fatal termination, though in one case it was followed by a marked remission of the symptoms —J K

HYPOPHYSIS extract as a heart tonic (*Zur Verwendung von Hypophysenextrakt als Herztonikum*) Pohl (A), Deutsche med Wchnschr (Berlin), 1921, 47, 1162

A patient, with cancer of the breast, who had a very weak pulse was greatly benefited by pituitrin injections Injections of camphor and caffein were without effect Pituitrin did not work so well in other cases In a hysterical girl complaints of "weakness" ceased when pituglandol was regularly administered —J K

Roentgen therapy in two cases of HYPOPHYSEAL dystrophia adiposogenitalis (*Zwei Falle von hypophysärer Dystrophia adiposogenitalis und ihre Behandlung mittels Röntgenbestrahlung*) Rauschburg (P), Deutsche med Wchnschr (Berlin), 1921, 47, 1291-1292

I A man of 19 presented severe headaches, giddiness, vomiting, typical eye symptoms (papillitis), a skiagram of the sella showed that the anterior clinoid processes were shorter than normal and that the dorsum sellae had disappeared Loss of libido sexualis, small thyroid and loss of hair were also features X-ray treatment resulted successfully First the headaches and vomiting disappeared, the vision became much better and the hairs began to grow again Hypophysis tablets were then given at the same time The patient was able to begin his work again

II A woman of 50 had adiposity, papillitis of both eyes, and headaches On the skiagram the sella showed somewhat deeper than normal Though she was blind, in this case x-ray treatment resulted in brilliant success The vision became 5/10 in both eyes—J K

Tumor of HYPOPHYSIS Schloffer, Wiener klin Wchnschr, 1921, 34, 518

Demonstration of a patient in whom a malignant adenoma of the hypophysis had been removed by the endonasal route Slight improvement of the eye symptoms followed No other details are given —J K

Cyst of the duct of the HYPOPHYSIS (*Hypophysengangzyste*) Schuster, Berl klin Wchnschr, 1921, 58, 682

A patient showed atrophy of the optic nerve No symptoms of acromegaly or dystrophia adiposogenitalis were found Radioscopy showed a small sella turcica At post-mortem a cyst of the duct of the hypophysis was found —J K

MIGRAINE, its cause and treatment Wolfe (S), Northwest Med (Seattle) 1921, 20, 288-291

The author considers an endocrine fault as a possible basis for migraine, but can not yet indict any one of the internal secretions specifically. Our knowledge of endocrinology is still so vague, that neither in the etiology nor in the therapy of migraine, can we do more than grope, when we attempt explanations or relief. Pituitary headaches are recognized but not considered true migraine. Migraine usually appears at about the time of puberty and is prone to disappear in women at the climacteric and in men about the same age.

—H L

PITUITARY standardization Tate (G), Pharm J, 1921, (4) 52, 268-269

The difficulties met in selecting a standard are cited. Different lots of U S P histamine standard may vary in activity. Histamine is depressant to the rat uterus, while infundibular extract is stimulant. Autolytic and bacterial changes in the slaughter houses might be detected by the use of a standard with the same action on the rat uterus as infundibular extract. In the excised uterus test on the virgin guinea pig, it was found that the results are changed by variations in the proportions of K and Ca in the Locke solution used, regular increases in the contractions were obtained by increasing the amount of KCl. Infundibular extracts deteriorate too quickly in the tropics to be employed as standards, samples sent out in March, 1920, and in September, 1920, had deteriorated to the same extent (30%) by February, 1921. The remaining activity was shown by tests on the rat uterus to be due to pituitrin and not to histamine. The amount of 1.5% KCl solution which had to be added to 60 cc Locke solution to produce a submaximal contraction of a portion of excised virgin guinea pig uterus was found to be 10 times the amount of 1:200 infundibular solution required to produce the same effect. The ratio is the same with different uteri, although different amounts can be used. The same amount of KCl is required to produce equal contractions whether in 1.5% or 15% solutions. The latter is more convenient, as the amounts are the same as the amount of infundibular extract solution to produce the same results. If more of the extract solution than of 15% KCl solution is required to produce the same submaximal contraction, then the extract is below standard. The same applies to the excised uterus of the virgin rat. An excess of CaCl₂ in the Locke's solution antagonizes the KCl. The contraction produced by KCl has slightly less lifting power than that due to infundibular extract.—Chem Abst, 15, 2336

PITUITRIN Van den Bergh, Vox Medicorum (Utrecht), 1921, 21, 153-154

When pituitrin is given where there is a strict indication, it is a splendid obstetric aid —J K

Intermediate processes in DIABETES INSIPIDUS and their significance (Ueber intermediäre Vorgänge beim Diabetes insipidus und ihre Bedeutung für die Kenntniss vom Wesen dieses Leidens) Veil (W), Biochem Ztschr (Berl), 1918, 91, 317-389

Diabetes insipidus is an individual disease characterized by the symptom complex of polyuria, polydipsia, low concentration of urine and changes in the intermediary water and salt relations. The lowered concentration of the urine is to be recognized as a practical symptom of variable value. The studies were carried out on patients having the disorder. According to the type of metabolic disturbance observed it appears as if there are two fundamentally different diseases which can be classed as hyper-osmotic and hypo-osmotic diabetes insipidus. In the former the ability of the organism to retain its water is lost. In the latter the whole organism is on another lower osmotic level. Studies of the intermediary exchanges of salt and water showed that the trouble is not renal, but principally due to tissue anomalies. The kind of relation supposed to exist between the nervous system and the internal secretions on the one hand and diabetes insipidus on the other is completely unknown. The extracts of the posterior lobe of the hypophysis are by no means specific in their action —F S H

The HYPOPHYSIS in the pathogenesis of diabetes (Ueber die Bedeutung der Hypophyse in der Pathogenese des Diabetes mellitus) Verron (O), Zentralbl f allg Path u path Anat (Jena), 1921, 31, 521-531

Description of 6 cases of diabetes with exact post-mortem reports

1 Atrophy of the pancreas, goiter, both lobes of the hypophysis enlarged, in the pars glandularis a largely increased number of eosinophil cells were found. The pars intermedia was normal, but with large vacuoles. The pars nervosa was normal.

2 The pancreas was normal, there were no changes in the islands of Langerhans. The hypophysis was small, without changes, except hyperemia of the pars anterior.

3 The pancreas showed arteriosclerosis and contained much fat. The islets were absolutely normal. In the hypophysis the pars intermedia was very small. The pars nervosa was normal, but contained many basophil cells. In the pars anterior were seen many mitoses.

4 The pancreas showed only unimportant sclerosis in some islets. In the hypophysis the pars anterior was small, the lobus posterior large. In the pars anterior a large number of eosinophil

cells and in the pars posterior, pigmentation was seen. The pars intermedia showed necrosis.

5 The pancreas was slightly atrophic. There were psammoma in the pars intermedia of the hypophysis.

6 Metastasis of a cancer was found in the hypophysis. The pars posterior and intermedia had been destroyed by the tumor.

The author believes that these cases prove the existence of hypophyseal diabetes. (He seems to be quite unaware of the evidence that changes in the hypophysis have no influence on metabolism and that changes in metabolism are due to pressure on the midbrain.)

—J K

HYPOPHYSEAL adiposity with psychic disturbance (*Hypophysäre Adipositas mit psychischer Störung*) Weggandt, *Deutsche med Wchnschr* (Berlin), 1921, 47, 881

Data reported elsewhere —J K

(HYPOPHYSIS) Changes in the cartilages of the larynx in acromegaly (*Veränderungen des knorpeligen Kehlkopfgerüsts bei Akromegalie*) Weingärtner, *Deutsche med Wchnschr* (Berlin), 1921, 47, 1111

In man complete ossification of the thyroid cartilage of the larynx is normal. In woman it is seen in cases of acromegaly with tumors of the hypophysis, but not in acromegaly without tumors in the hypophysis —J K

Tumors of HYPOPHYSIS with special reference to symptoms (*Contributio alla conoscenza dei tumori dell' ipofisi con particolare riguardo alla loro sintomatologia*) Zino (A), *Gaz d Osped* (Milano), 1921, 42, 740-743

Description of three cases with the ordinary symptoms of headache, giddiness, loss of vision and changes in the sella turcica —J K

INFANTILISM in children Leebron (J D), *Penn M J* (Harrisburg), 1921, 24, 810-812

The classification of Gilford is referred to, and then a brief description follows of atellosis and progeria, in which the etiology is unknown except that the cases are familial and hereditary. The symptomatic group includes Herter's intestinal infantilism, Bromwell's pancreatic infantilism, the Lorrain type, the Brissaud variety, the Froelich syndrome. The last three are probably due to insufficient thyroid or pituitary secretion. Finally come the retarded development and growth associated with congenital heart disease, malnutrition from tuberculosis, arterial hypoplasia, lymphatic diathesis, congenital lues. The importance of radiograms of the hand in diagnosing delayed ossification is emphasized. Thyroid extract according to Leebron, is often helpful —H L

A case of INFANTILISM with enuresis (Ein Fall von Infantilismus mit Enuresis) Tromner, Deutsche med Wchnschr (Berlin), 1921, 47, 1179

A girl of 16 weighed 28 kilograms, with a height of 135 cm. There was no hair on the pubes or in the axillae, and menstruation was absent. The diagnosis was polyglandular infantilism. This patient suffered also with enuresis and had a slight spina bifida
—J K

Calcium metabolism and INTERNAL SECRETIONS (Kalkstoffwechsel und innere Sekretion) Bauer (J), Wien klin Wchnschr, 1921, 34, 314-315

A general review without new data —J K

Antithrombin an INTERNAL SECRETION of nuclear origin (Méchanisme régulateur de la fluidité du sang Existence d'une sécrétion interne d'origine nucléaire) Doyon (M), Médecine (Paris), 1921, 2, 918-922

One of the factors in the maintenance of fluidity of circulating blood is an internal secretion known under the name of antithrombine. This substance is a nucleoprotein active in vitro. Its origin is in the cellular nucleus. All the nuclear acids exercise an anti-coagulant action in vitro. Their use allows of obtaining a stable plasma resisting the action of serum. In cats and dogs it is only the liver which appears to contain any antithrombine easily mobilisable, but it is possible that all organs because of their cellular nuclei are the starting point of the internal anti-coagulant secretion —R G H

(INTERNAL SECRETIONS) Secrezioni interne e sistema nervosa Laignel-Lavastine, Arch gen di neurol psych e psicolanal (Napoli), 1921, 2, 5-52

Republication in Italian of material reviewed in Endocrinology, 1919, 4, 342 —R G H

(LIPOID GLANDS) On glandular adipose tissue, and its relation to other endocrine organs and to the vitamine problem Cramer (W), Brit J Exper Path (Lond), 1921, 1, 184

While in most animals the naked eye appearance of body fat from different sites of the body is fairly uniform, in certain species of animals, as, for example, the white rat and the tame mouse, two distinct types of adipose tissue can be recognized (1) the ordinary yellowish-white fat, (2) reddish-brown masses. The three most important masses of the second type occur (a) between the scapulae with extensions between the muscles, (b) in the thorax in front of the vertebral column along the thoracic aorta, (c) in the abdomen between the kidneys along the aorta, extending upward enclosing

the suprarenal glands and downward enclosing, in the female, the ovaries. These fatty organs differ from ordinary adipose tissue in being rich in "lipoids," especially cholesterol and its compounds, and in having a very rich blood supply. Cramer suggests that these lipid-rich fatty organs be designated "lipoid glands" or "cholesterin glands." Reasoning by analogy, he further suggests a relationship between these lipid glands and the suprarenal cortex. He has made some observations which suggest that these lipid glands are concerned in the problem of vitamins and deficiency diseases

—D M

Contribution to the study of cerebral metabolism by the method of partial circulation. IV. Internal secretion of the LIVER and morphological variations of the cerebral neurones. Renauld-Capart (H), Arch intern de physiol (Paris), 1921, 16, 119-161

It is concluded that it is necessary for the blood to circulate through the liver if cerebral activity is to continue. It is suggested that the liver affords this facilitation either through a detoxicating process or because of the elaboration of a specific internal secretion. The latter hypothesis is supported by the evidence. Moreover, when hepatic function is arrested there is produced in the cerebral neurones a condition of chromatolysis, which is succeeded by a chromatophile regeneration corresponding with the return of function of the centers when the blood supplying the brain is allowed to pass through the liver. The statement is made "Cerebral metabolism in its entirety, psychic effort and conscious perception, are directly dependent on an internal secretion of the liver, elaborated as a thermolabile substance, the action of which seems to facilitate the continuous formation of the chromatophile substance of the neurones"—Chem Abst, 15, 2115

(MENOPAUSE) The prognosis in high blood pressure. Graham-Stewart (A), Practitioner (London), 1921, 107, 183-200

The author briefly refers to the high blood pressure often encountered in women at or near the menopause. Of all types, he considers this group most amenable to treatment. "The underlying pathology is probably an endocrine disturbance, associated with emotional states and a hypersensitivity of the nervous and vasomotor systems"—H L

A case of MYOTONIA DYSTROPHICA (Ein Fall von myotonischer Dystrophie). Full, München med Wchnschr, 1921, 68, 1064

A man of 46 had dystrophy of the muscles of hands, forearms and of the sterno-cleido-mastoid, together with facies myopathica. Hypoplasia of the thyroid was noted. Probably the endocrine disturbance as well as the myotonia are both due to changes in the involuntary nervous system.—J K

(ORGANOTHERAPY) Treatment of sterility by means of organic extracts Bercovitch (A), Med Rec (New York), 1921, 99, 1052-1055

A first essential is to be reasonably sure that the sterility in a given case has an endocrine origin, second, to recognize the ductless gland chiefly responsible, and whether it is secreting too much or too little. The close functional correlation of thyroid, anterior pituitary and ovaries is emphasized. The pituitary type originating prior to or after adolescence and the preadolescent hypothyroid and ovarian types are briefly described. Then follows brief records of nine patients, illustrative of the above types, all women, suffering from partial or complete amenorrhoea, with or without obesity, or dysmenorrhoea. Depending on the organ chiefly at fault they were given thyroid extract, or pituitary anterior lobe, or ovarian extract. No pluriglandular preparations were administered. Menstruation returned, or was normally regulated in all of them, and pregnancy followed each case, though most of them had been married and sterile for many years. (The author is to be congratulated on his remarkable success. Since many others have been by no means as fortunate in their results, one is tempted to inquire how many cases were unsuccessfully treated, so that the percentage of cure could be ascertained.)—H L

(ORGANOTHERAPY) The treatment of the chronic intestinal invalid Bryant (J), Am J M Sc (Phila), 1921, 161, 74

In discussing the hyposthenic variety of subjects with gastrointestinal manifestations, Bryant devotes a page to glandular therapy. Whole gland suprarenal preparation in five grain doses is used in certain cases of chronic exhaustion. Bryant is convinced that in these cases better results are obtained with than without this preparation. In many instances, he also finds one-tenth and one-fourth grain doses of thyroid useful. In women ovarian preparations are certainly of value in selected cases.—J F

(ORGANOTHERAPY) A psychological study of some mental defects in the normal dull adolescent Clark (L P), Med Rec (New York), 1921, 99, 991-996

A sentence is devoted as follows to the ductless gland aspect: "While there are still chances for a wider and more exact extension of endocrinology in mental defects, as yet it has not materially altered the general statement that once a definite determination of any degree of feeble-mindedness has been made in a child, the condition which remains is hopeless so far as recovery or cure is concerned"—H L

Concerning the result of the active factor in ORGANOTHERAPY for menstrual disorders (Ueber die Erfolge und das wirksame

Prinzip der Organextrakttherapie bei Menstruationsstörungen)

Esch (P), Zentralbl f Gynak (Leipzig), 1920, 44, 561-568

Esch calls attention to the apparently paradoxical results so often observed with organotherapy. In the case of the ovary, for example, he refers to the good results reported by various authors from the administration of ovarian or corpus luteum extract in cases of hyperfunction of the ovary, especially the functional hemorrhages of puberty and those of later life. On the other hand, the same preparations are reported to give satisfactory results in cases of hypofunction, as in amenorrhea. He brings out similar paradoxes with pituitary therapy. His explanation of these matters is that we are not dealing in organotherapy with specific secretions, but that the results are due to factors of non-specific nature. He is impressed with the work of Kohler, who obtained, with Enteroglandol, an extract of the intestinal mucosa, results in the treatment of amenorrhea which were similar to those following the use of luteoglandol, a corpus luteum preparation. Biedl has also observed the similarity of toxic symptoms produced by various organ extracts with those of peptone poisoning. Esch has treated a number of cases of menstrual disorder, especially menorrhagia, by the parenteral (intramuscular) administration of protein bodies, such as breast milk. These observations support his hypothesis that the action of the organ extracts is of a non-specific protein nature.—E N

Carcinomatous dermoid cysts of the OVARY (Karzinomatöse Dermoidzysten des Ovariums)

Eisenstädter (D), Monats f Geburtsh u Gynäk (Berlin), 1921, 54, 360-366

Not of endocrine nature.—F S H

The specific secretion of the OVARY (Ueber das spezifische Ovarialsekret)

Fellner (O O), Zentralbl f Gynäk (Leipzig), 1920, 44, 1133-1138

This article is a reply to that of Esch (q v). Fellner insists upon the fact that the "feminine sexual lipoid," previously described by him, is the specific secretion of the ovary. The characteristic lipoid can be demonstrated in the placenta, the corpus luteum, the interstitial cells of the ovary, and the testis, but not in any other tissue. Its subcutaneous injection in animals produces enlargement of the uterus, oestral changes in the endometrium, and hypertrophy of the breasts. Fellner criticizes the well-known work of Seitz, Wintz, and Fingerhut, who isolated from the corpus luteum two substances which predominate at different phases of the corpus luteum cycle and the physiological action of which is quite antagonistic (lipamin and luteolipoid). He alludes briefly to some interesting studies which he and Neumann had carried out on the effect of x-rays upon the ovaries of pregnant rabbits. These appear to indicate a definite secretory role for the interstitial cells.—E N

Does our present knowledge of the structure and function of the **OVARIES** support the theory of the internal secretion of the **CORPUS LUTEUM** and the **INTERSTITIAL GLAND** (Stutzt unsere jetzige Kenntniss uber den Bau und die Theorie der inneren Sekretion des Corpus Luteums und der Interstitiellen Druse)? Garlund (W), Zentralbl f Gynäk (Leipsic), 1918, 42, 649-663

The author reviews the evidence for the internal secretory activity of the corpus luteum and the interstitial glands, and finds that it is, on the whole, inconclusive. For example, he believes that the premenstrual swelling of the endometrium, commonly attributed to the activity of the corpus luteum, might just as logically be explained as due to the periodic hyperemia associated with the maturation and later nidition of the ovum. He also finds fault with the view of Fraenkel that the corpus luteum exerts a trophic control over the uterus, for, as he says, the uterus is not atrophic in those animals which have no periodic corpus luteum of menstruation. As a result of the study of sudan-stained tissue he believes that many of the histological changes in the corpus luteum and interstitial glands are explainable as granulation processes. He argues also that it is unnecessary to assume a specific hormone activity because of the finding of sudan-stained lipoid granules, and that this assumption is not justified either on histological, clinical or experimental grounds. The article is decidedly hypercritical, but quite suggestive.—E N

Experimental physiological action of OVARIAN extracts Gofalons (G P), Surg Gyn & Obst (Chicago), 1918, 26, 196-206

After reviewing the work of previous investigators upon the influence of ovarian extracts on the circulation, Gofalons reports the results of his own personal studies. He used macerated decoctions and extracts in different solvents—alcohol, chloroform, ether—of ovaries without corpus luteum and of the corpus luteum of the cow, and from animals of 1, 2 and 3 years. The ovaries were used as quickly as possible after being obtained from the slaughter houses, in some cases in 3 or 4 hours, in others within 12 hours. In the latter case they were preserved in a refrigerator at 0°C or frozen. Maceration was effected with physiological solution or Ringer-Locke fluid 1/4 or 1/5, triturated, macerated during one-half to one hour and then filtered through cotton. Decoctions were made by boiling 5 or 10 minutes. The author has noted no difference in the actions of corpus luteum extract from gravid and non-gravid animals. Immediately after the injection of doses of 20 cc of maceration or decoction of gravid corpus luteum at 1/4 or 1/5, there is a marked hypotension of 50, 60, 70 or even 80 mm of mercury. The pressure falls rapidly, cardiac pulsations are generally considerably weakened, and there are sometimes in the first moments deep convulsive

respirations After 1, 2 or 3 minutes the pulsations strengthen and the pressure rises This is relatively rapid at first After 5 or 10 minutes the pressure returns to normal Respiration is momentarily accelerated, then becomes normal The effect on the heart is a diminution in the amplitude, with generally a tachycardia In rabbits toxic or subtoxic doses cause peristaltic contractions perceptible beneath the skin The uterus of guinea pigs shows a marked hyperemia Finally, the author reports clinical and experimental evidence as to what he considers a strongly galactagogue action of ovarian extracts—E N

(OVARY) Corpus luteum and the periodicity in the sexual cycle
Loeb (L), Science (Garrison, N Y), 1918, 48, 273-277

This paper is largely a review of the work of the author and others upon the subject "We can at least be certain that the living corpus luteum has the function of inhibiting ovulation and of being a decisive factor in the mechanism of the sexual cycle"—Chem Abst, 14, 970

On the physiological correlation between the OVARIES and the uterus (De la corrélation physiologique entre les ovaires et l'utérus) Nielsen (F), Compt rend Soc de biol (Paris), 1921, 85, 368-369

Using the method of Leo Loeb, the author studied the reactions of the rabbit's uterus against intervention, under different physiological conditions (1) When the uterine segment was opened 3 to 7 days after ovulation, when the corpus luteum should be developing in the ovary, "placentomes" appeared at the point of opening (2) Contrary to Loeb's findings in the guinea pig, irritation of the mucosa with a glass rod 3 to 7 days after ovulation never caused decidual alterations in the rabbit (3) When the operation was made 3 to 7 days after copulation, not having given place to ovulation and consequently without the formation of the corpus luteum, no "placentomes" were formed, but "pseudoplacentomes", recurving of the edges of the incision toward the mesentery, and the simultaneous "proloration" of the uterine mucosa, presenting a diffuse hypertrophy (4) Extirpation of the ovaries or of the newly formed corpora lutea at the time of opening the uterus, 3 to 7 days after ovulation, is followed by the formation of "pseudoplacentomes" analogous to those mentioned above (5) In castrated females treated before and after opening the uterine segment with extracts of corpus luteum as well as extract of the ovarian interstitial gland, intravenously, the opening of the uterine segment gave rise to the formation of "pseudoplacentomes," while opening the uterine wall was followed by cicatrization without prolapsus or hypertrophy of the mucosa—T C B

A further study of the end-results of the conserved OVARY Polak (J O), Am J Obst (New York), 1918, **78**, 199-211

Polak refers to a previous study of 132 cases, from which he concluded that a conserved ovary, if unhealthy, will leave the patient in a worse state mentally, nervously and physically than if total extirpation had been done, that total ablation is preferable at or near the menopause, and that the symptoms of the operative menopause are less after extirpation for pelvic inflammation than when the ablation is done for fibromyomata. The present paper is based on a study of the pathology found in 73 re-operations for clinical suffering and subsequent disease in the retained ovary. Polak describes a technic for the conservation of the ovary after removal of the uterus, without interfering greatly with the blood supply of the ovary. From the study of more than 300 patients followed for 5 years, he finds that the average duration of the ovarian function after hysterectomy is not over 2 years, and that within that time, flushes and dizziness occur in the large majority. The fact that 73 women had to be re-operated upon within 5 years convinces Polak that routine conservation of the ovary or a part of the ovary, when the uterus has been removed, is not always in the best interests of the woman. The lesions which were found in the retained ovary at re-operation were multiple cystic changes, cirrhosis, cystic formation, infection, and thin-walled cysts with dense adhesions.—E N

(THYROID) The medical treatment of Graves' disease, with special reference to the use of CORPUS LUTEUM extract Hoppe (H H), J Nerv & Ment Dis (New York), 1918, **47**, 254-261

The theory on which Hoppe bases the use of extract of corpus luteum in Graves' disease is that the latter and hyperthyroidism are synonymous terms, that the internal secretion of the corpus luteum has an inhibitory effect on the thyroid, and that hyperthyroidism is an expression of a dysfunction of the corpus luteum in the female and of the interstitial glands of the testis in the male. He is apparently willing to accept the view of Claude and Gougerot that Graves' disease is due to hypovarial disease. He has treated about 20 cases of Graves' disease according to this plan. He found the combination of quinine hydrobromate, *ext belladonnae* and *ext corpus luteum* to be rapidly beneficial in nearly all the cases. He considers the corpus luteum to be the active therapeutic agent.—E N

The absence of PANCREATIC secretions in sprue and employment of pancreatic extract in the treatment of the disease Brown (T R), Am J M Sc (Phila), 1921, **161**, 501-507

Brown has found a complete absence of pancreatic secretion in all five cases of sprue studied. In all instances, he gave pancreatic

or some form of pancreatic extract, in five to ten grains dose along with twenty to forty grains of calcium carbonate or lactate three times daily two hours after the larger findings. Marked improvement occurred in four cases presented as long as treatment was continued. This was true of one case which was under observation for several years. Her well being is absolutely dependent upon the administration of the pancreatic ferment. The fifth case showed no benefit from this treatment —J F

Cystadenoma of PANCREAS (*Zystadenom des Pankreas*) Ghon, *Munchen med Wehnschr*, 1921, 68, 1134

Of no endocrine interest —J K

Cysts of the PANCREAS Judd (E S), *Collected Papers Mayo Clinic*, 1920, 12, 406-415 (Reprinted from *Minnesota Med*, 1921, 4, 82-90)

A discussion of the frequency and a general discussion of the pathology, clinical features, and treatment of cysts of the pancreas. The paper is based upon a series of forty-one cases that occurred in the Mayo Clinic. The conclusions are that the condition is rare, does not produce a definite syndrome, is associated with gall bladder diseases in more than one-third of cases, and is amenable to surgical procedure —J F

PANCREAS tumors (*Zur Klinik der Pankreastumoren*) Kleinschmidt (K), *Deutsche med Wehnschr (Berlin)*, 1921, 47, 1162-1163

Of no endocrine interest —J K

PANCREAS and HYPOPHYSIS Kraus (E T), *Wiener klin Wehnschr*, 1921, 34, 505

Data reported elsewhere

Diagnosis and treatment of diseases of the PANCREAS with special respect to diabetes (*Diagnostiek en interne therapie von pancreasstoornissen en met bijzondere betrekking tot de diabetes*) Peutz (J L A), *Inaug Diss (Utrecht)*, 1921

An excellent review of the literature with beautiful microphotographs. The author states that although the pancreas has an influence on sugar metabolism yet there are many cases of diabetes in which no change in the pancreas is observed. The pancreas may be the seat of the origin of diabetes, but certainly it is not the only organ able to produce diabetes mellitus —J K

Studies on PANCREATITIS (*Beiträge zur Lehre von der Pankreatitis*) Schoenig (F), *Mitt a d Grenzgeb d Med u Chir (Jena)*, 1921, 34, 101-111

Of no immediate endocrine interest —J K

Totalsequestration des PANCREAS Schutt, Berl klin Wchnschr 1921, 58, 1012

A patient of 52 gradually became ill with pain in the upper abdomen, intermittent constipation and fever. There was a fluctuating tumour in epigastrium. The urine contained 5% of sugar. At operation a large abscess cavity was found between the stomach and liver, the bottom of the abscess was formed by the necrotic pancreas. Recovery followed —J K

PANCREAS concretions (Konkrementbildungen im Pancreas) Simmonds, Berl klin Wchnschr, 1921, 58, 1013

In 8 of 11 cases of pancreas stones the patients died of coma diabeticum. It is perhaps possible to diagnose these cases by radiography —J K

The PANCREAS in Hodgkins disease and DIABETES of old age (Le pancréas dans la maladie de Hodgkin et dans le diabète aisé des vieillards) Sloboziano (H), Ann méd (Paris), 1921, 9, 362-376

A histological study of the pancreas of 9 patients. In one person with Hodgkin's disease the organ was found to be pathological. In the 8 cases of senile glycosuria the pancreas was also pathological —F S H

Investigations on the hydrogen-ion concentration of blood after the copious ingestion of acids or of bases, and during the tetanic attacks following the extirpation of the PARATHYROID glands (Recherches sur la concentration du sang en ions hydrogène apres ingestion abondante d'acides ou de bases, et pendant les attaques tétaniques consecutives a l'extirpation des glandes parathyroïdes) Ege (R) & Henriques (V), Compt rend Soc de biol (Paris), 1921, 85, 389-391

The greater part of the report deals with changes in pH in the blood of normal goats and dogs. Ingestion of acid (HCl) over a twenty-four day period, displaced the pH decidedly to the acid side. On the other hand, sodium bicarbonate shifts the pH to the alkaline side. Of endocrine interest is the fact that after removal of the parathyroids and thyroid, during attacks of tetany the pH is reduced below the normal, agreeing very well with that found in man during intense muscular work —T C B

(PARATHYROID) General osteitis fibrosa Fraenkel (E), Deutsche med Wchnschr (Berlin), 1921, 47, 1147

In this case one of the parathyroids weighed 4.9 gm. Histologically, the tumor consisted of normal parathyroid tissue. The author believes that the experimental work on tetany has only a very limited clinical value. He has almost never found pathological changes in cases of tetany. When it is true, as experiments have shown, that the parathyroids have an influence on calcium metabolism, it is possible that there really exists a relation between parathyroids and osteitis fibrosa. However, only very few cases are known. A similar case has been reported by O. Meyer.—J. K.

(PARATHYROID) Report of a case of tetany after the third partial thyroidectomy. Gessner (H. B.), New Orleans M. & S. J., 1921, 74, 382-384.

The case is interesting in that the symptoms were very severe and that parathyroid, as well as calcium, medication failed to relieve them. When bromid was added to the calcium the symptoms were ameliorated.—R. G. H.

Transplantation of PARATHYROIDES in paralysis agitans (Ueber die Transplantation von Nebenschilddrüsensubstanz bei der Paralysis agitans). Kuhl (W.), München med. Wchnschr., 1921, 68, 1083-1084.

In a case of Parkinson's disease the author prescribed tablets of parathyroid, as recommended by Camp, without any success. In another case, however, a splendid result was obtained by transplanting two parathyroids of the calf. (It may be noted that this case was operated on the 5th of July, 1921, and has been reported on the 26th of August).—J. K.

(PARATHYROID) General osteitis fibrosa. Simmonds, Deutsche med. Wchnschr. (Berlin), 1921, 47, 1147.

In this case there was a struma parathyreoidea, the size of a hazelnut. The author considers this goiter as the cause of the bone disease, and compares this to the acromegaly which is caused by a struma of the hypophysis. It would perhaps be possible in cases of osteitis fibrosa to examine the parathyroid in a surgical way and to remove tumors when present.—J. K.

A note on the cytology of the PINEAL body of the sheep. Jordan (H.), Anat. Rec. (Phila.), 1921, 22, 275-285.

The "interneuroglial cells" of the pineal body of sheep from four to eight months of age are characterized by an abundance of small spherical mitochondria and a variable number of larger lipid globules. These lipid globules constitute the only cytologic evidence indicative of a secretory activity.—W. J. A.

New studies on the PINEAL gland (Neue Studien uber die Zirbel-druse) Marburg (O), Arb a d neurol, Inst a d Wien Univ (Leipzig and Wien), 1920, 23, 1-35

An article which contains many interesting statements, but which should be read with a critical sense The author holds that the pineal is definitely an endocrine organ having an influence on sexual precocity, metabolism and the vasomotor activities It is stated that hyperfunction of the pineal induces adiposity Certain therapeutic suggestions are made, which, however, do not seem to be founded on more than inference —J K

Tumor of the PINEAL gland Morquio (L), Arch Lat-Am de Pediat (Buenos Aires), 1919, 13, 119-127

Morquio's patient was a boy of 12, previously healthy until he began to complain of headache and the clinical picture of tuberculosis meningitis became installed, quite typical, except that the spinal fluid seemed to be normal The child died at the end of a month, and necropsy revealed sarcomatous changes in a tumor in the pineal gland, probably of congenital origin —See also *Endocrin*, 3, 78 —J Am M Ass, 73, 156

PLACENTAL tissue as a galactagogue Cornell (E L), Surg Gyn & Obst (Chicago), 1918, 27, 535-538

The preparation used by Cornell is made from the placenta of cows The placenta is washed and dried, and then put up in 5 grain capsules The dose found most satisfactory is 5 grains four times a day The first dose is given as soon as the patient is able to take nourishment and has had a rest from labor, usually within 12 hours after delivery No bad effects were noted on the gastro-intestinal tract, although some few patients objected to the odor of the preparation A table is given showing the results obtained in 100 cases The study seems to have been satisfactorily controlled The author concludes that placental tissue has a favorable effect on the production of milk The nationality or age of the patient plays no part, nor does the sex of the baby Eighty-seven per cent of the babies whose mothers had received placental tissue began to gain on the fourth and fifth days, against sixty-nine per cent whose mothers did not receive the medication Forty-four per cent of the experimental subjects regained their birth weight before leaving the hospital against twenty-four plus per cent of the controls —E N

Cytological studies on the internal secretory functions in the human PLACENTA and decidua Fujimura (G), J Morphol (Phila), 1921, 35, 485-578

A comprehensive study from the cytological viewpoint An extensive bibliography is appended Abundant morphological evi-

dence is adduced to show that the placenta is a source of internal secretions. This is true, however, only for the earlier months of pregnancy. Later there is little to indicate the possession of endocrine functions. The epithelium and stroma of the chorionic villi, the decidual cells and the uterine glandular cells, which constitute the chief tissue elements of the placenta and decidua, have received minute attention. All of these show the formative elements of secretions such as plastosomes, lipoid granules and vacuoles. All, except the last, are believed to form internal secretions. The manner of the formation and the discharge of the secretions is described. It is noted that, of all the secretions, those which come from the syncytial layer, decidual cells, uterine glandular cells (a part) and also probably from the Langerhans' islets are absorbed by the mother's body, while those which pass from the ordinary Langerhans' cells and the stroma of the villi are absorbed by the fetus. It has been believed by several authors that the epithelium of the chorionic villi probably serve as an organ by which nutrition is taken up by the embryo. Fujimura, however, states that histologically it is impossible to find any ground for such belief.—W. J. A.

The importance of renal glycosuria for the early diagnosis of PREGNANCY (Ueber die Verwendbarkeit der renalen Schwangerschaftsglykosemie zur Frühdiagnose der Gravidität) Nurnberger (L.), *Deutsche med. Wchnschr.* (Berlin), 1921, 47, 1124-1126.

Frank and Nothmann have stated that alimentary glucosuria after the ingestion of 100 grams of glucose may often be a very early symptom of pregnancy. The difference between this glycosuria and the glycosuria as seen in cases of diseases of the liver, latent diabetes, thyrotoxicosis, etc., is that in pregnancy the rise of the blood sugar after 100 gm. glucose remains within normal limits. Nurnberger has confirmed these statements in studies of 71 patients. In all cases the symptom described by Frank and Nothmann was positive. In one case of pregnancy a pathological hyperglycemia after ingestion of glucose was found. In another case the reaction was positive without pregnancy. In cases of abortion the reaction remained positive as long as large parts of the placenta in the uterus were in connection with the uterine wall. When, however, the embryo lies loose from the uterine wall the reaction is negative.—J. K.

Action of PROSTATE extracts Sellei (J.), *Ztschr. f. Urol.*, 1918, 22, 183.

Prostate extracts had no action on the prostate itself, and in other respects their action was barely appreciable.—*Phys. Abst.*, 3, 144.

SCLERODERMA ameliorated by thyroid (Scléremie des adults, amélioration par le traitement thyroïdien) Darier, Ferrand & Mir

couche (Mlle), Bull Soc frang dermat et syphil , 1919, —, —,
(No 5), Abst , Schweiz med Wchnschr (Basel), 1919, 50, 1052

A case is reported of generalized scleroderma following shock and grippe There was no sclerodactyly Improvement followed the administration of thyroid —R G H

SCLERODERMA Pulay (E), Deutsche med Wchnschr (Berlin), 1921, 47, 1247

Demonstration of a case of scleroderma with sclerodactyly Pathogenesis is unknown, in this case the generative organs were hypoplastic, menstruation was irregular, the calcium content of the blood was increased and there was much perspiration Dysfunction of the thyroid is probable —J K

SCLERODERMA Viehweger, Munchen med Wchnschr , 1921, 68, 861

The author studied the Abderhalden reaction in some cases of scleroderma In one case the reaction was positive with thyroid, in the others with hypophysis In one of these patients a good effect was obtained by intramuscular injection of extract of hypophysis It was never possible to detect adrenalin in the blood with the Meltzer-Ehrmann reaction —J K

The SPLEEN and digestion Study I The spleen and gastric secretion Inlow (Wm De P), Am J M Sc (Phila), 1921, 162, 325-348

The author presents a comprehensive review of the literature upon the role of the spleen in digestion This is followed by the presentation of his experimental data and his conclusions His data on gastric secretion were obtained upon three dogs with accessory stomach pouches (secretion meal of meat) before and after splenectomy and on two similar dogs serving as controls Removal of the spleen in these experiments caused no noteworthy changes in gastric secretion except a slight diminution in the quantity of gastric juices obtained The author concludes from his data and the review of the literature that a definite pepsinogenic function of the spleen has not been demonstrated and that the relation is probably merely vascular —J F

Transplantation of the TESTICLES (Zur Frage der freien Hoden-transplantation) Haberland (H F D), Zentralbl f Chir (Leipz), 1921, 48, 993-994

Haberland has used a disk cut from the testicle for transplantation as recommended by Payr He performed this operation in hares and has noted that when such a disk was removed the sexual functions remained normal or became normal some time

later In one animal a disk was removed from one testicle, the sexual functions returned $2\frac{1}{2}$ months after the operation When such a disk is transplanted it is always resorbed after a time Still this is no ground for holding that transplantation would be useless The author suggests the idea that whilst the graft is resorbed other endocrine organs may take its function In double castration this process is too acute to enable the other endocrine organs to assume the functions of the testicles As the structure of cryptorchid testicles is not identical with the structure of a normal organ, transplantation of cryptorchid testicles is not recommended —J K.

(TESTES) Case of melancholia treated by Steinach's operation (Ueber eine nach Steinach operierte Melancholie) Kramer, München med Wchnschr, 1921, 68, 194

A report of a case of melancholia in which double vasectomy was performed, with consequent amelioration From the short description afforded, however, one is led to the opinion that this success is rather due to the optimism of the author than to a real improvement of the patient —J K

(TESTES) A case of melancholia treated by vasectomy (Eine nach Steinach operierte Melancholie) Kramer, Deutsche med Wchnschr, (Berlin), 1921, 47, 1082, Berlin klin Wchnschr, 1921, 58, 1058

The patient, a man of 59 with a severe melancholia, was suffering from hypertrophy of the prostate, sexual impotence and moderate glycosuria Bilateral vasectomy was performed Immediately after the operation restlessness, agitation, irritability and negativism appeared After two months marked improvement was evident The patient became brighter, gained weight and had more appetite, slept better, again had erections and once even an ejaculation The urine was free from sugar After the demonstration of this patient Wiener reported that he had treated the patient and has noted a spontaneous remission The patient is not cured, the glucosuria had disappeared many months before the operation Lowry has also observed the same patient and does not consider him as cured —J K

(TESTES) Transitory sexual impotence in conscripts and its cure (Impotencia sexual transitoria en conscriptos y su curacion) Lopez (Julio A), Semana méd (Buenos Aires), 1921, 28, 350

The author has observed that sexual impotence is quite frequent in young conscripts of 20 years He attributes this condition to intoxication from alcohol and tobacco The oral administration of testicular substance produced benefit —B A H

(TESTICLE) Thyrogenital pluriglandular dystrophy (*Distrofia pluriglandulare prevalentemente tiroo-genitale a tipo di juvenilismo persistente*) Mariotti, *Riforma med* (Naples), 1919, 35, 590-596

Mariotti reports a case of testicular dystrophy with definite symptoms of pituitary hyperactivity and thyroid insufficiency in a man aged 21. A portion of a healthy testicle removed from a man in whom total emasculation had been performed on account of epithelioma of the penis was grafted beneath the skin of the flank and was followed by a rapid improvement in the genital functions. The improvement, however, was confined to the genital sphere, and was of short duration. At the end of a year no trace of the testicular graft remained, and the patient's condition had become the same as before. Mariotti regards the failure of the operation as an additional argument for maintaining the pluriglandular origin of these syndromes. In such cases it is best to treat the cause of the dystrophy, which in the present case was tuberculosis.—*Med Sc Abst & Rev*, 2, 135

TETANY Bossert, *Berl klin Wchnschr*, 1921, 58, 1055

Of no endocrine interest—J K

THYMUS (*Dermatosis und innere Sekretion*) Brock, *München med Wchnschr*, 1921, 68, 191

The author believes that there exists a relation between psoriasis and the thymus. Especially in psoriasis, but also in lichen ruber planus, ichtvosis, etc., he recommends exposure of the thymus to x-rays—J K

(THYMUS, THYROID) Goiter heart and cardiac changes in status thymicolymphaticus (*Zur Frage des Kropfherzens und der Herzveränderungen bei Status thymicolymphaticus*) Fahr (Th) & Kuhle (J), *Virchow's Arch f path Anat [etc]* (Berlin), 1921, 233, 286-301

Report of six cases in three of which there were myocardial changes. In the gross the major characteristics were cardiac dilatation and paleness of the muscle. Microscopically there were found round cell infiltrations of varying intensity associated with increased numbers of eosinophils and inflammatory edema. Degenerative changes in the muscle cells and vessel walls as noted previously by Wiesel were also observed. The authors think these myocardial changes are manifestations of the action of a systemic toxin and that the entire anatomical picture of status thymicolymphaticus is best interpreted as only a symptom of some still unknown chemical change—D M

(THYMUS) Roentgen therapy in intrathoracic lesions with special reference to status thymolymphaticus Meyer (W H), *Arch Pediat* (New York), 1921, 38, 572

Retrogression of the thymus with clinical cessation of symptoms is obtainable within a period of from one to four months. Providing dosage be exact, failure of symptomatic relief suggests an error in diagnosis. The effect of properly measured roentgen dosage on the thymus appears so definite that it might be applied as a diagnostic procedure in doubtful cases. Meyer gives the technic as used at the New York Post Graduate Hospital. Improvement was noted in nearly every case of thymus involvement —M B G

The influence of exposure of the THYMUS to x-rays on the excretion of uric acid (*Ueber die Beeinflussung der Harnsaureausscheidung durch Rontgenbestrahlung der Thymusdrüse*) Pother & Szego
Wien klin Wchnschr, 1921, 34, 386

The authors submitted the thymus of normal individuals and of patients with Graves' disease to the action of x-rays. In some cases of Graves' disease the excretion of uric acid was increased after this treatment. It is stated that this increased quantity of uric acid is a proof of an enlarged thymus —J K

Lipoma of the THYMUS (*Zur Lehre der Thymushpome*) Yamanoi (S), Zentralbl f Chir (Leipz), 1921, 48, 785-787

A lipoma of the thymus was found in a woman dying of uraemia. This is the second case described —J K

(THYROID) Manic depressive psychosis (*Manisch-depressives Irresein*) Arndt, Deutsche med Wchnschr (Berlin), 1921, 47, 1180

Arndt believes that this disease is due to an endocrine disturbance, especially of the thyroid. Therefore, psychotherapy has so little success —J K

The relation of normal rats with and without THYROID feeding and of thyroidectomized rats to oxygen deficiency (*Das Verhalten von normalen, mit Schilddrüsensubstanz gefütterten und schilddrüsenlosen Ratten gegen reinen Sauerstoffmangel*) Asher (L) & Duran (M), Biochem Ztschr (Berl), 1920, 106, 254-274

The authors have carried further the work of Streuli, who showed that normal, thyroidectomized and splenectomized rats behave differently in the presence of a deficiency of oxygen. Normal and thyroidectomized rats behave nearly alike and withstand reduced oxygen pressure well while splenectomized rats are much more sensitive and more injuriously affected. In addition to confirming Streuli's results they add their results on the effect of thyroid feeding. The method consists of putting the animals under a bell jar, gradually reducing the pressure and noting the behavior of the animal, particularly as regards its respiration. They report in detail

three experiments carried out on thyroidectomized rats and five experiments on normal rats which had been fed with thyroid. They find that normal rats fed with thyroid are as sensitive to reduced oxygen pressures as are splenectomized rats. This effect was detectible in five days after beginning the feeding. They point out that inasmuch as thyroid feeding produces the same effects as splenectomy that this is further possible evidence of an antagonistic action between the thyroid and spleen and that this phenomenon may have some bearing on the etiology of Basedow's syndrome. They further point out that the effect of thyroid feeding on the ability of rats to withstand oxygen deficiency could be used as a biological test for the pharmacological activity of desiccated thyroid.

—D M

(THYROID) Hyper- and hypo-thyroidism, causation, prevention and treatment Barr (J), Practitioner (London), 1921, 106, 381-399

The author, for instance, has "long since discarded" x-rays or operative treatment of exophthalmic goiter, believing that "simpler, less expensive and more effective methods should suffice." Of the latter he strongly advocates Albert Abram's concussing of the 6th and 7th cervical spines, as a means of contracting the left ventricle and making far more effective systole. The hyperactive calcium metabolism should be diminished. Alkalinization of the blood is advised. Phosphoric and citric acids as decalcifying agents are recommended. In early cases of hypothyroidism iodine is our sheet anchor, in advanced cases thyroid extract should be added, and where there is retention of calcium salts, decalcifying agents should be administered. Barr regards adenoids as due to defective thyroid function and believes that a lump of solid iodine should be placed in a current of air in the children's dormitory as a prophylactic. Enlarged prostate is considered analogous to a large fibroid goiter and associated with defective thyroid function, and thyroid extract, iodides and decalcifying agents and restriction of lime intake, is indicated. (A jolly, chatty article, more entertaining than scientific) —H L

(THYROID) Iodine in the treatment of goiter Beebe (S P), Med Rec (New York), 1921, 99, 996-999

The importance of the iodine content of the thyroid normally and in the goitrous gland is discussed. The author then states that in his experience three different forms of iodine answer all the requirements for therapeutic purposes, namely, potassium iodide, ferrous iodide, and thyroid extract. The writer has never been able to find any advantage in the large array of ointments, organic compounds of iodine, or so-called colloidal preparations of iodine available in the market. He has had no experience with Kendall's thy-

roxin Beebe strongly deprecates large doses of iodide in any form of goiter, even ten grains three times daily In endemic or simple goiter one or two grains three times daily should be used at first, gradually increased to five grains three times daily, rarely, if ever, is it necessary to give larger doses Beebe does not favor the large doses advocated by McCarrison Furthermore, the iodine should be administered for a long time, months and even years Quite opposed to prevailing opinion, the writer believes iodine to be one of the most valuable therapeutic agents we have in the treatment of the hyperthyroid forms of goiter If the dose is properly regulated there need be no fear of iodine Basedowism The hyperplastic gland is poor in iodine—0.095 milligrams per gram of fresh gland, as against 0.364 in normal thyroids The dosage recommended is one-half to one grain of potassium iodide three times daily to begin with and for several weeks or months following Especially is iodine beneficial in women who have had exophthalmic goiter for several years "No other medication can replace iodine in this group"

—H L

(THYROID) Exophthalmic goiter as a cause of sterility (*L'accroissement d'une cause de stérilité féminine depuis la guerre par le développement de la maladie de Basedow*) Blondel (R), Bull Acad de méd (Paris), 1919, 3 s, 82, 185-188

Blondel comments on the prevalence during the war of the emotional factors known to co-operate in the production of exophthalmic goiter, and remarks that he has not been surprised to find hyperthyroidism much more prevalent now than in former years, especially in women Any one of the main symptoms, the exophthalmos, the tachycardia, tremor or goiter, may alone reveal the excessive functioning of the thyroid, and explain any one of numerous trophic and other changes Chief among these he has noticed a decrease in the size of the uterus This atrophy of the uterus is possibly the explanation of sterility in certain cases, and as such the causal hyperthyroidism should be combated There are several ways of doing this, raying the thyroid, injecting serum from thyroidectomized animals, thymus treatment, and other means He prefers thymus treatment, and has been using it for years as the routine treatment in exophthalmic goiter He gives half a raw thymus from a lamb, chopped and mixed with a little flour, salt and butter to make small balls that are mixed with soup as it is eaten Subcutaneous injection of the extract is more active, but less convenient for the patient Thymus treatment is logical, he reiterates, on account of the antagonism between the thymus and thyroid, and years of experience have proved the soundness of these premises He warns in conclusion that we must be wary in giving iodine in cases of amenorrhea or we may whip up an incipient exophthalmic goiter The thymus treatment in these cases of sterility might be supplemented by massage

of the uterus and dilation with laminaria for three or four days, each month or two months. The pathologic condition does not seem to be able to right itself spontaneously but with this treatment perseveringly carried out good results were obtained in the majority of his cases—*J Am M Ass*, 73, 1808

THYROIDITIS in scurvy (*Thyroïdite au cours du scorbut*) Bonnet (P), *Gaz d hôp*, 1920, 93, 376, *Abst Med Sc Abst & Rev* (Lond), 1920, 3, 10

Bonnet reports the case of a Roumanian farmer who developed acute suppurative thyroiditis during an attack of scurvy. The localization of the infection in the thyroid was probably due to small hemorrhages in the gland becoming infected from the septic buccal cavity—*R G H*

Report of a case of INFANTILISM with rickets Boyd (D H), *Penn M J* (Harrisburg), 1921, 24, 870-875

A remarkable case of infantilism in a girl of 6 years is reported. There were some bony changes and other symptomatology of rickets, but also complete filling of the sinuses with solid bone, and absence of sella turcica in x-ray plates. Pancreatic efficiency tests gave normal results and feeding with pancreatic extracts was unsuccessful. The patient did not correspond to any of the recognized endocrine types, such as infantile myxedema, Froelich's preadolescent hypopituitarism or Lorain infantilism. Some of the signs and symptoms suggested osteogenesis imperfecta, fragilitas osseum and leontiasis ossea, but none of these diagnoses was warranted. Boyd was finally disposed to consider the case one of intestinal infantilism with rickets and with a secondary hypophyseal involvement to account for the hyperostosis in the skull. Treatment directed to rickets, to ductless gland disease and to intestinal infantilism (as advised by Herter), were all ineffectual. Complete autopsy findings revealed hypoplasia or atrophy of the hypophysis, pineal, thymus, thyroid, and adrenals, amyloid disease of the liver, spleen, and kidney, hemorrhage from intestine, liver, and gall bladder, fatty infiltration of the liver, generalized edema, general hyperplasia of the bony structures of head, face, ribs, and extremities, with spontaneous fractures of the left radius and left femur—*H L*

The influence of THYROID extract on the multiplication of cells (*L'action de l'extrait thyroïdien sur la multiplication cellulaire*) Champy (Ch), *Arch de Morph gén et expér* (Paris), 1922, 1, 1-58

Tadpoles were put into basins of water with large quantities of dried thyroid of sheep. It was observed that when after 48 hours the animals were taken out and placed in clear water, they were "sensibilised." In other words, the effect of the thyroid seemed to

continue The limb buds, when studied histologically, showed a change in the "coefficient mitotique" This coefficient is obtained by observing, in at least 4,000 cells, the numbers with and without mitosis It does not vary much in normal tadpoles during growth In animals treated with thyroid this coefficient for cells in the skin of the limb buds steadily increases until the death of the animal The same is observed in the muscles and the cartilages of the limbs In the intestines, however, the opposite is seen The normal regression with degeneration of epithelium is hastened In the tongue, esophagus, stomach and thymus, the number of mitoses rapidly increases by thyroid treatment Proliferation is found in the nervous system, but only for a limited time and in special places, e g, in the encephalon These facts are held to prove that extract of thyroid exerts not a general, but a selective influence Its action depends not only on the presence of a hormone, but also on the local sensibility of the various tissues —J K

(THYROID) Treatment of goiter (Kropfbehandlung) Eiselsberg, Munchen med Wchnschr, 1921, 68, 894

The etiology of goiter is unknown The cause should always be sought Before operation radiosopic examination in two planes is desirable Only in this way is it possible to get an idea of the shape of intrathoracic goiters Almost complete thyroidectomy is advisable The danger of tetany is not negligible When it occurs it is advised not to begin with parathyroid transplantation, but to try injections of afenil, lactate of calcium up to 30 grams daily, and clysmata with chloral hydrate When transplantation is necessary the organs ought to be taken from children dying at birth Histological examination of the organ is necessary Even slight tetany has a doubtful prognosis, as the symptoms may rapidly increase The best treatment of Graves' disease is resection of the thyroid Thy-mectomy, according to the author, not necessary The operation should be performed under narcosis, the patient should take calcium lactate a long time before the operation, and be kept quiet The author considers the thyroid as the primary seat of Graves' disease

—J K

The THYROID gland and exophthalmic goiter Foss (H L), Penn M J (Harrisburg), 1921, 25, 35-39

A concise, conservative summary of our present knowledge of the thyroid, especially directed to a consideration of the diagnosis and surgical treatment of Graves' disease, nothing new is presented, but the review is well written —H L

(THYROID) Observations on the basal metabolism estimations in the goiter clinic of the university hospital Frazier (C H) & Adler (F H), Am J M Sc (Phila), 1921, 162, 10-12

This paper reports the experience of the University (Pennsylvania) Clinic with the portable Benedict apparatus in the study of goiter. The authors conclude that these estimations are of value in following ways. In eliminating those cases which will not be benefited and might be made worse by operation, in offering confirmatory evidence of the degree of toxicity, and in offering a quantitative index for use in diagnosis, prognosis, and treatment—J F

(THYROID) Treatment of goiter with x-ray (Behandeling van struma met Röntgenstralen) Gaarenstroom (G F), Ned Tijdschr v Geneesk (Haarlem), 1921, 65, 209-214

In goiter or Graves' disease x-rays nearly always produce an improvement or cure. The vasomotor and nervous symptoms diminish or disappear and metabolism becomes normal. This is particularly true in malignant goiter. The symptoms of pressure rapidly improve, and if no metastases are present splendid results may be obtained. In the 15 cases reported by Gaarenstroom 7 were of the exophthalmic type and 4 were cancerous—J K

(THYROID) Tumors of liver with the structure of a colloid goiter (Lebertumoren vom Typus einer Kolloidstruma) Godel (A), Munchen med Wchnschr, 1921, 68, 1003

From a woman of 21 a colloid goiter was removed. Sixteen years later a tumor was found in the abdomen. It proved to be a colloid goiter in the liver. Some months after this operation the woman died from an embolus in the arteria pulmonalis after childbirth. At post-mortem examination many tumors were found in the liver, all showed the typical structure of a colloid goiter—J K

(THYROID) Intralaryngeale Struma Godel (A), Munchen med Wchnschr, 1921, 68, 1002

Data are to be reported in full in the Arch f Laryngol—J K

(THYROID) Typical changes in the blood under the influence of want of oxygen (Ueber ein typisches Verhalten des Blutes unter dem Einfluss der Sauerstoffmangels) Gutstein (M), Folia haematologica (Leipzig), 1921, 26, 211-230

When too small quantities of oxygen are available for the tissues typical changes in the blood occur. Whether oxygen deficiency is caused by a small quantity of oxygen in the air, as in the mountains, by diseases of the lungs or by destruction of erythrocytes, the changes in the blood picture are the same. As the number of erythrocytes increases the amount of hemoglobin becomes higher, the neutrophilic leucocytes diminish, and lymphocytosis with eosinophilia is observed. But the same blood picture is observed in Graves' disease (not at all typical—J K) and hyperthyroidism. We know also that want of oxygen has an influence on the thyroid, for Mansfield and

others have proved that the typical blood picture in the mountains is not observed in animals when the thyroid has been previously removed. Therefore, Gutstein concludes that the influence of a want in oxygen in the blood is mediated through the thyroid, which is stimulated in turn and gives rise to the changes in the blood —J K

Congenital teratoma of the THYROID (Kongenitales Schilddrüsenteratom) Hadda, Berlin klin Wchnschr, 1921, 58, 1084

In a new born baby with tumor of thyroid and attacks of suffocation the tumor was removed. Histologically, thyroid tissue, central nervous system tissue, cylindrical epithelium, cells resembling intestinal glands, muscles, and connective tissue were found —J K

(THYROID, THYMUS) X-ray treatment of scleroderma (Zur Röntgenbehandlung der Sklerodermie) Hammer (G), München med Wchnschr, 1921, 68, 1109-1110

That scleroderma has some relation to endocrine disorders is made probable by cases of the disorder accompanied by symptoms of Graves' or Addison's disease. In a patient with thyreotoxicosis, who had scleroderma of the hands and forearms, the symptoms disappeared after exposure of the thyroid to x-rays. In another patient with sclerodactyly with changes in the bones no effect was seen from exposure of the thymus and thyroid to x-rays. In a third patient with scleroderma, a small goiter, and now and then tachycardia, a marked improvement followed radiation of the thymus and thyroid —J K

(THYROID) Metabolimetry in hyperthyroidism Harrower (H R), Med Rec (New York), 1921, 99, 1003-1005

A concise statement of the use of basal metabolism estimation in the diagnosis and treatment of thyroid disease, more especially hyperthyroidism, together with reference to those who are chiefly responsible for the development of this procedure —H L

(THYROID) Maladie de Basedow familiale et héréditaire chez l'enfant. Harvier (P), Paris méd, 1919, 9, 457-459

In Harvier's case the goiter developed at 12, and the young man's mother, grandmother and an aunt on both the maternal and paternal sides had presented exophthalmic goiter. His sister had escaped. The tremor in his case had been noted from early childhood —J Am M Ass

Chemical studies of physiology and pathology. Function of the THYROID gland (Chemische Studien zur Physiologie und Pathologie Zur Funktion der Schilddrüse) Herzfeld (E) & Klinger (R), München med Wchnschr, 1918, 65, 647-651

A series of experiments carried out on rats to which was fed a preparation of thyroid proteins iodized by the authors. The results lead to the conclusion that the secretion of the thyroid hormone is not tied up with a protein body, but is concerned with a dialysable decomposition product. The iodine is considered as being in the gland in the form of a salt combination of the protein decomposition product, it is not an actual constituent of the secretion, but its function is rather to facilitate the formation of the secretion. The nerves of the gland act to increase the hydrolytic processes in the cells

—F S H

Comparative sensitivity to intoxication and infection of animals deprived of the THYROID (*Sensibilidad comparada de los animales tiroprivos a la intoxicación y a la infección*) Houssay (B A) & Sordelli (A), *Rev Asoc méd argent* (Buenos Aires), 1921, 34, 435

Thyroidectomy does not modify the sensitivity of the rabbit toward diphtheria bacilli or toxin nor that of the guinea pig toward diphtheria or cobra toxin. The rabbits which have trophic symptoms and a poor state of nutrition are most sensitive.—B A H

Influence of the THYROID on the formation of antibodies (*Influencia de la tiroides sobre la formación de anticuerpos*) Houssay (B A) & Sordelli (A), *Rev Asoc méd argent* (Buenos Aires), 1921, 34, 438

Rabbits deprived of the thyroid produce a serum hemolytic toward sheep, more active than that of the controls. Rabbits and horses deprived of the thyroid produce an agglutinating serum slightly more active than the controls (Eberth). The results are more complex in regard to the production of antitoxin for the dog deprived of thyroid produces immune sera (antidiphtheritic and antitetanic) a little more active than those of normal dogs. Rabbits, and above all horses, deprived of the thyroid produce a serum very feeble in power compared to that of controls.—B A H

Histological changes in the central nervous system in THYROIDECTOMIZED cats (*Histologische Veränderungen im Zentral-Nervensystem bei Schilddrüsenmangel*) Isenschmidt (R), *Frankf Ztschr f Path* (Weiss), 1918, 21, 321-336

The cytology of the central nervous system was studied in cats which had been thyroidectomized from two to four months previously. Basic aniline dyes, methylene blue, thionin and toluidin blue were used. Isenschmidt found the most marked changes in the more differentiated cells, as, for example, the motor cells of the anterior horn and the Purkinje cells. He noted particularly a decrease in the number and a shrinkage in the size of the Nissl granules. He points out, however, that such changes as he has observed cannot be

considered as characteristic of thyroid deficiency since similar changes are found in a great variety of intoxications —D M

Creatin metabolism and the THYROID gland (Kreatinstoffwechsel und Schilddrüse) Iseke (C), Monats f Kinderh (Berlin), 1921, 21, 337-350

The author reports a series of studies on the creatin excretion in children, particularly in its relation to thyroid activity. He confirms the presence of a physiological creatinuria in children, disappearing at about the age of 12-14. In a normal infant of 4 months he found that the creatin comprised 87% of the total creatin-creatinin excretion. The creatin excretion was definitely influenced by the degree of thyroid activity present. In cases of myxedema the creatin excretion was diminished or even absent, and he considers this an early and diagnostic test for athyreosis. In a case of hyperthyroidism he found an increased creatin excretion and in myxedema the creatin excretion was increased by thyroid feeding —C H G

Metamorphosis provoked by the injection of THYROID preparations and of THYROXIN (Kendall) in thyroidectomized Axolotls. Heightened toxicity of iodized combinations in the case of thyroidectomized animals (Métamorphose provoquée par l'injection de préparations thyroïdiennes et de thyroxine (Kendall) a des Axolotls ayant subi la thyroïdectomie. Toxicité élevée des combinaisons iodée dans le cas d'animaux thyroïdectomisés) Jensen (C O), Compt rend Soc de biol (Paris), 1921, 85, 391-392

The author has shown that metamorphosis may be provoked in Axolotl not only by specific thyroid substance, but also by injection of iodocasein, iodoserumglobulin and iodoserumalbumin. Intraperitoneal injections of thyroxin (synthetic) also determines metamorphosis. Is this metamorphosis due to the direct effect of the compounds, or is the effect indirect, the compound being absorbed by the thyroid, and transformed? Iodized combinations are very toxic for thyroidectomized axototl. Doses too small to effect metamorphosis kill the animal, and therefore the above question must remain unsolved at present. Experiments with thyroxin, however, favor the hypothesis that it is the hormone of the thyroid gland.

—T C B

(THYROID) Struma maligna Kuijter (J H), Ned Tijdschr v Geneesk (Haarlem), 1921, 65 (II), 1133-1134

Demonstration of a case, markedly improved by x-ray treatment —J K

Action of the THYROID and the PARATHYROID glands on respiratory exchange (Action du corps thyroïde et des glandes parathyroïdes sur les échanges respiratoires) Labbé (M) & Stévenin (H), Ann méd (Paris), 1921, 9, 264-270

The authors studied the respiratory exchange in a series of normal, parathyroidectomized and thyroidectomized rabbits, and rabbits to which desiccated thyroid was administered. Two parathyroids were removed from the experimental animals. Although the respiratory quotient for the four groups remained the same within the limits of the methods employed, there is evident from the tabulated results a decided influence on the oxygen consumption and CO₂ production as a result of the procedures described. There is an increase in these factors in the parathyroidectomized and thyroid fed animals and a decrease in the thyroidectomized rabbits. Although the increase is slight in the parathyroidectomized group it seems as valid as are the other variations. The possibility of an antagonistic action of the two glands is expressed.—F S H

THYROID and other endocrine disturbances as viewed by the internist Lichty (J A), *Am J M Sc (Phila)*, 1920, 159, 800-814

Early recognition and prompt action are urged for the successful medical treatment of hyperthyroidism. For advanced cases the roentgen ray is recommended as presenting attractive advantages in application.—W J A

The pathogenesis of deficiency diseases. The effects of some food deficiencies and excesses on the **THYROID** gland. McCarrison (R), *Indian J Med Res*, 1920, 7, 633-647

The effects on the thyroid apparatus of imperfect, ill-balanced and excessive diets have been studied in monkeys, guinea pigs and pigeons. The diets used may be grouped according to their effects on the histology of the thyroid gland under two headings: (1) those that induce a decrease in the size and weight of the thyroid, and (2) those that induce an increase in the size and weight of the thyroid. Under Group 1 (diets inducing a decrease) the following diets were used: (a) autoclaved milled rice, (b) autoclaved rice and butter, (c) autoclaved rice, butter and onion, (d) autoclaved food and onion, (e) autoclaved food and butter and onion. All five of these diets have vitamin deficiencies and all cause a diminution in size and weight of the thyroid. Under Group 2 (diets producing thyroid enlargement) the following diets were used: (a) crushed oats and autoclaved milk, (b) mixed varieties of millet seeds, (c) mixed varieties of millet seeds, peas, butter, with and without onion. The enlargement found in guinea pigs fed on the scorbutic diet of oats and autoclaved milk was found to be due largely to congestion and hemorrhagic infiltration. The thyroid enlargement from overfeeding with millet seeds is a true hypertrophy and hyperplasia. Still more marked hypertrophy and hyperplasia were observed when butter and peas were added to this diet. The addition of onion to this high protein and fat diet appeared to lessen the thyroid hyperplasia. The author believed the beneficial effect of onion in retarding hyper-

plasia is due, in part at least, to its action in restraining the growth of putrefactive bacteria in the gastrointestinal tract and in retarding the absorption of their products, while diets deficient in vitamins render the thyroid gland susceptible to the noxious action of intestinal bacteria or their products, with resultant atrophy and necrotic changes. He seems to have realized the dangers from uncontrollable factors in evaluating the data of such experiments —D M

(**THYROID**) Simple goiter a public health problem McCord (C P) & Walker (R C), Ohio State M J (Columbus), 1920, 16, 501-506

See Endocrin, 4, 499

The **THYROID** and its diseases Mayo (C H), Collected Papers Mayo Clinic, 1921, 12, 323-329 (Reprinted from Surg Gyn & Obst, 1921, 32, 209-213)

A review of the progress made in this field. The value of basal metabolic rates, blood pictures, epinephrin injections as diagnostic means are discussed as well as the factor which lessens the dangers of operation —J F

(**THYROID**) Endemic and sporadic cretinism (Ueber endemischen und sporadischen Kretinismus) Melzer, Berl klin Wchnschr, 1921, 58, 1019

Endemic cretinism is due to geological causes. Sporadic cretinism or infantile myxedema has probably no relation whatever to geological conditions, but is due to degeneration of the thyroid. In endemic cretinism the thyroid often shows hypertrophic degeneration, though normal areas may be found. Sporadic cretinism generally begins in youth and produces symptoms resembling those of myxedema. Thyroid, fresh or in tablets, is beneficial —J K

(**THYROID**) Case of cachexia strumipriva (Fall von Cachexia strumipriva) Mobius, Berl klin Wchnschr, 1921, 58, 1017

A man of 36 was operated upon for the third time for goiter. Though a part of the goiter was left behind, myxedema developed. The voice became rough, the hair fell out, the patient felt weak and tired, and the skin was swollen and dry. Thyroid tablets had a good effect. The tissue removed showed colloid goiter with much connective tissue. Probably the piece left behind had not sufficient functional capacity to prevent the onset of myxedema —J K

(**THYROID**) Endemic goiter in Urubamba (Peru) [El bocio endémico en Urubamba (Peru)] Monge (C), Cron Méd (Lima), 1920, 37, 394-415

Monge attempted to determine whether the endemic goiter of Peru is, like that of Brazil, due to a trypanosome and transmitted

by an insect A study of the blood of sixty persons in the goiter belt of Peru failed to reveal the presence of this organism Inoculations into animals gave negative results The drinking water is the principal vehicle of propagation, but there is no danger when it is boiled The germ of Chaga's disease was never found present

—A M Q

(THYROID) Basedow's syndrome, and cretinism in Urubamba (Peru) [Syndromes Basedawiano, y cretinismo en Urubamba (Peru)] Monge (C), Cron Méd (Lima), 1921, 38, 3-11

Monge describes different kinds of goiter with hyper- and hypothyroidism, and cretinism as frequently found in Urubamba, Peru

—A M Q

Diagnostic and clinical aspects of HYPERTHYROIDISM (Diagnostico y aspectos clinicos de hipertiroidismo) Mora Quimper (A), Cron Méd (Lima), 1921, 38, 170-176

The author considers the need in the clinic of an early diagnosis of hyperthyroidism at a time when it is quite impossible to find any tumor in the thyroid gland The different criteria of diagnosis, as Goetsch's ephrinephrin test, the changes in the blood sugar, the high metabolic rate, and the variations in the blood picture, before and after the Goetsch test, are very valuable for an early diagnosis of this trouble, as well as for the removal of these patients from the neuropathic group where they are sometimes placed Some clinical aspects of hyperthyroidism, especially its cardiac and nervous aspects, are considered —Author's Abst

(THYROID) Sporadic hemophilia successfully treated with hemato-ethyroidin Acute thyroiditis during the treatment (Hemophilic sporadique traitée avec succès par l'hémato-éthéroidine Thyroïdite aigue au cours du traitement) Oddo (C) & Mattei (Ch), Bull et mém soc méd des hôp d Par, 1921, 45, 1292-1298

A report of a case concisely described in the title Hemato-ethyroidin was given in the dose of 3 spoonfuls in coffee per diem After 47 hours all hemorrhage had stopped After 6 days of treatment there was fever, rapid pulse, dysphagia and redness over the right lobe of the thyroid in which could be felt a tumefaction as large as a nut Exophthalmia was present On the 7th day the fever began to subside as did the swelling in the thyroid Epistaxis reappeared, to subside on the readministration of the drug, which again caused the development of the hyperthyroid syndrome The patient has been under observation now for 2 years and has continually improved —F S H

(THYROID) Surgery of sub-sternal and intrathoracic goiters Pemberton (J de J), Collected Papers Mayo Clinic, 1920, 12, 354-375

A comprehensive clinical surgical paper based upon the experiences of the Mayo Clinic in handling this type of goiter. The results of the operation for removal of these goiters were very satisfactory. The mortality was low and the patients were almost immediately relieved of most distressing symptoms —J F

Gout and THYRO-TESTICULAR insufficiency (Goutte et syndrome thyro-testiculaire) Phronimos (S), Thèse de Paris, 1918

From a review of literature and a good description of a clinical case the author comes to the following conclusions. Gout and insufficiency of the thyroid and testicles may be observed in one and the same patient, although this combination has, up to the present, never been described. Some years before the patient was attacked with gout, endocrine disturbances were evident in easy fatigue, loss of sexual desires, atrophy of the testicles, and loss of hairs of the axilla and pubes. The administration of testicle extract had a bad effect, when given alone, thyroid was well taken and when combined with testicle yielded a good result. The gout pains were markedly better some time after treatment with thyroid had been instituted. The author states that clinicians should note the possibility of endocrine disturbance in cases of gout —J K

The value of basal metabolism studies in the diagnosis and treatment of THYROID diseases Rowe (A H), Am J M Sc (Phila), 1921, 162, 187-200

A summary of the literature concerning the clinical value of the test, together with the author's own data. Eighty cases have been studied by the Tissot spirometer-gas analysis method. The author's conclusion serves to re-emphasize the importance of basal metabolism determination in the handling of thyroid diseases. By this method diagnosis of early and obscure cases is facilitated. It is of special value as a guide in treatment —J F

(THYROID) The value of Bram's quinine test as a diagnostic measure for exophthalmic goiter (Sur la valeur du test de Bram a la quinine comme moyen de diagnostic du goitre exophthalmique) Sainton (P) & Schulmann (E), Bull et mém soc méd des hôp d Par, 1921, 45, 1304-1306

The authors consider that this test should be accepted with only the most severe reservations. This opinion is supported by studies on 10 cases —F S H

(THYROID) Glycemia and hyperglycemia produced in exophthalmic goiter (La glycémie et l'hyperglycémie provoquée chez les sujets atteints de goitre exophthalmique) Sainton (P), Schulmann (E) & Justin-Besançon, Bull et mém soc méd des hôp d Par, 1921, 45, 1298-1303

Studies on glycemia in Basedow's disease demonstrate that hyperglycemia is not constant in the disorder and is of low degree that there is no relation between the glycemia and the intensity of the Basedow's disease, whether it is a question of induced or normal glycemia. The results of induced hyperglycemia, whether produced by ingestion of glucose or injection of hypophyseal extract, are inconstant and no different from those obtained in other pathological conditions. Adrenine hyperglycemia is more frequent after glucose ingestion, but there is no relation between the reaction and the reaction to pituitrin in the same subject. The action of the thyroid in carbohydrate metabolism is an unsolved problem. The occurrence of exophthalmic goiter and diabetes has as yet not been proven to be more than coincidence.—F S H

(THYROID) Basedow's disease (Ueber den Morbus Basedow)

Schmidt (O), Mitt a d Grenzgeb Med u Chir (Jena), 1921, 33, 512-532

A highly important study. The author attempted to determine if the distinction between thyroidism and Basedow's disease is an artificial one. He, therefore, examined the blood in these cases. The blood picture in Basedow's, in thyroidism and in normal individuals, whether thyroid is given or not, shows no characteristic difference. R. Schmidt has stated that parenteral administration of proteins produced in Basedow's disease a much more marked thermal reaction than in other conditions. The author could not confirm this. Complement fixation tests with extracts from exophthalmic goiter thyroids or jodothylin used as antigens proved to be useless. A cutaneous reaction with extracts of exophthalmic goiter thyroids gave no reliable results. However, it was found that the freezing-point of the serum in Basedow's disease is much lower than that of normal sera. In thyroidism it proved to be higher than in normal sera. When the patients with Basedow's disease are kept in bed, the freezing-point shows a tendency to become normal. Operation ought never to be carried out as long as the freezing-point of the serum is not normal. There is another difference between the serum in Basedow's disease and in thyroidism. Kottmann has described the "dispersion power" (Dispergierungsvermögen) of serum. This means the power with which the serum prevents a substance in colloidal state from precipitation. Kottmann used iodide of silver. The technic is as follows. To 1 cc of serum (taken after a short fast) is added 0.25 cc of 5% K I and 0.3 cc of 5% Ag NO₃ solution. This is done in the dark. A white precipitate is formed. This is exposed for 10-25 minutes to an intense light. Then 0.5 cc of 0.25% hydrochinone is added, after which the color becomes red, brown and at last black. In Basedow's disease it takes 5-7 hours before the serum is black, in normal individuals this time is much shorter, in thyroidism still shorter. It is remarkable that in diseases of the pancreas, in Addison's disease,

and in hypophyseal disease this time is longer than normal, though never as long as in Basedow's disease. The author concludes that thyroidism is a different disorder from Basedow's disease. He considers thyroidism as an intoxication with incomplete, and Basedow's disease as an intoxication with excess products of the thyroid.—J K

(THYROID) The indications for surgical treatment in the various types of goiter. Sistrunk (W E), Collected Papers Mayo Clinic, 1920, 12, 330-336 (Reprinted from Surg Gyn & Obst, 1921)

All goiters are divided into colloid, adenomatous, and exophthalmic. Colloid goiters in young persons are looked upon as not surgical. In the majority of instances, after patients with adenomatous goiter have attained the age of 25 or 30, surgery is advocated. All adenomatous goiters associated with hyperthyroidism are considered surgical if the condition of the patient will permit an operation. Exophthalmic goiter, according to their experience, is best treated surgically. If care is exercised in selecting the type of operation to be performed in a given case, the mortality following the operation is low.—J F

(THYROID) The surgical treatment of goiter (Ueber die chirurgische Behandlung des Morbus Basedow). Sudeck (P), Deutsche med Wchnschr (Berlin), 1921, 47, 1224-1226, Berl klin Wchnschr, 1921, 58, 1050

The diagnosis of "Graves' disease," according to Sudeck, is too often made. Especially the diagnosis of "formes frustes" is much abused. He distinguished three types of hyperactive thyroid disease. 1 The classical Graves' disease, with highly vascularized goiter and proliferation of epithelium in the gland. 2 Thyroidism with colloid goiter, with the typical histological picture of a non-vascularized goiter and no proliferation of epithelium. Often the "thyroid heart" is found. The symptoms are the same as when too much thyroid is administered. They develop more slowly, whilst the real Graves' disease has a more acute character. Though many authors deny a difference between these types, Sudeck maintains that they are not identical. 3 Status neuropathicus. Here there exists often a colloid goiter with symptoms of physical and psychical degeneration. The symptoms are very variable, including abnormal irritability, vasomotor disturbances, headaches, giddiness, tremors, but no exophthalmus. The blood picture as described by Kocher is often found. In this last type surgical treatment rarely is successful. The other types must be treated by ligation of the four arteries and resection of both lobes of the thyroid. In five cases of very serious Graves' disease the author has completely removed the thyroid and given thyroid preparations afterwards. In all these cases the results have been good, though once tetany was seen after the operation. Sudeck does not believe that, though in special cases it

may be necessary, thymectomy is generally indicated. X-ray treatment never has the same splendid effect as operation, and as there are adhesions formed, and cases known in which this treatment produced myxedema, the author warns against it —J K

(THYROID) Observations on goiter Sweet (P W), Northwest Med (Seattle), 1921, 20, 105-109

Sweet classifies goiters as follows I Colloid—(a) adolescent, (b) simple colloid II Adenoma—(a) non-toxic, (b) toxic III Hyperplastic, exophthalmic, always toxic IV Carcinomatous He briefly presents the pathological pictures and symptomatology and clinical course of these types and their differentiation He believes that the first group are always non-surgical unless pressure symptoms should be very disagreeable The other three groups he considers always surgical and does not even refer to possible medical or x-ray treatment The various stages of operative procedure in very toxic cases are mentioned, namely, boiling water injections, preliminary ligation of one or more vessels and finally thyroidectomy —H L

Small THYROID tumor accompanying incomplete syndrome of Basedow's disease, with osseous metastases (Syndrome de Basedow incomplet chez une malade ayant une petite tumeur thyroïdienne avec métastase osseuses) Tixier (L) & Duval (H), Bull et mém soc méd d hôp de Par, 1921, 45, 875-877

The authors report the case of a woman of 67 years who was much emaciated Tremor and tachycardia were evident A small tumor of the left lobe of the thyroid was palpable In view of the distribution of metastases in the osseous system the thyroid tumor was considered malignant and to be the cause of the symptoms of Basedow's disease —F S H

Creatin metabolism and the THYROID (Kreatinstoffwechsel und Schilddrüse) Tseke (C), Monats f Kinderh (Berlin), 1921, 21, 337-350

Creatin is found in the urine of normal children of 1½ years In hypothyroidism creatin fails to be found in urine of children Of course if the only symptom found in a child is a lack of creatin this is not enough for a diagnosis of hypothyroidism Nevertheless, it is an important symptom In hyperfunction of the thyroid in children the urinary creatin is generally increased Also in Graves' disease the quantity of excreted creatin is high, also in fever, toxicosis and in serious diabetes As a test for the activity of thyroid preparations the author recommends observation of its influence on the amount of creatin in the urine of children This must be markedly raised

—J K

The influence of THYROPARATHYROIDECTOMY upon blood sugar content and alkali reserve Underhill (F P) & Nellans (C T), J Biol Chem (Balt), 1921, 48, 557-561

The removal of the thyroid apparatus from dogs results in a lowered blood sugar content. There seems to be little or no change in the carbon dioxide capacity of the blood up to the onset of tetany. After this period there may be a decided tendency toward a diminished alkali reserve—F S H

(THYROID) Congenital goiter (Over aangeboren kropgezwollen) van Goor (W T), Inaug Dissertation, Amsterdam, 1921

Congenital goiter has never been described in the Dutch medical literature. Van Goor has now studied the weight of the thyroids of newly born children in Amsterdam (where goiter is not endemic). The average weight is 1.5 gram. In countries where goiter is endemic the average weight is much higher, even when no congenital goiter is found. In regions with endemic goiter the number of cases of congenital goiter is much larger than elsewhere. In a children's hospital in Berne in 22 years, 53 cases of congenital goiter were observed, in two of the largest hospitals in Amsterdam only 5 cases were seen in the same period. To avoid congenital goiter mothers during pregnancy often go to places which are free from goiter. Local circumstances certainly are of influence, but heredity also plays an important part. In many cases no cause can be detected. The histological structure of the congenital goiter varies widely, a typical picture does not exist. Congenital goiter always takes its origin from the thyroid proper. Goiters of the tongue, struma retrosternalis, etc., are never congenital. The weight of these goiters differ. In one case described it was 58 gm. They often contain cysts. Teratomas of the thyroid have been described. The author proposes the following scheme of classification. I Thyroid enlarged through hyperaemia—(a) goiter with hyperplasia of the blood vessels. II Hyperplastic goiters—(b) goiter with hyperplasia of the parenchyma, (1) solid follicles, (2) follicles with colloid, (3) follicles with papillary formation, (c) struma cystica, (d) struma fibrosa. III Teratoma of the thyroid. The symptoms of these goiters are dyspnoea or asthma neonatorum. The treatment must be surgical, three operations are possible: (1) to cut through the isthmus, (2) exothyreopexia, (3) strumectomy. Tracheotomy or intubation must be emphatically warned against—J K

(THYROID) Classification of goiter: an analysis of one hundred cases Williams (C), Am J M Sc (Phila), 1921, 161, 223-228

This paper attempts the correlation of the clinical histories and pathologic findings in 100 cases. The author further outlines the indications for surgical treatment of goiter. During the time selected

for study this clinic admitted 103 goiters and operated upon 100. The other three presented contra-indication for any surgical interference —J F

Malignant tumors of the THYROID Part I Wilson (L B), Collected Papers Mayo Clinic, 1920, 12, 376-385 (Reprinted from Ann Surg)

Nine hundred and seventy-one cases of malignant goiter are collected from the literature. The cases occurring in the Mayo Clinic are then reported as a group and analyzed as to clinical course, sex, age, and geographic distribution —J F

(THYROID) A malignant hemangio-endothelioma of the thyroid (Ein malignes Hamangioendotheliom der Schilddrüse) Winnen (P), Frankfurt Ztschr f Path (Wiesb), 1920, 23, 405-418

Reports case of 47 year old female with a large goiter of thirty years' standing which suddenly started to enlarge rapidly. Clinically a diagnosis of carcinoma of the thyroid was made. An operation performed and death followed ten days later. At necropsy it was found that the tumor locally had infiltrated the tracheal and esophageal walls. There were multiple metastases to the lungs. The author discusses at length the data for considering the tumor an endothelioma, all of which is purely morphological and therefore not absolutely convincing. It is well known that the thyroid tissue tumors offer peculiar difficulties as regards differentiation morphologically into sarcomas, carcinomas and endotheliomas —D M

(THYROID) Comparative study of the frequency of different forms of goiter in Basel and in Bern (Vergleichende Untersuchungen über die Häufigkeit der verschiedenen Knopfornen in Basel und in Bern) Woelz (E), Schweiz med Wchnschr , 1921, 51, 625

These observations are based on the surgical material from the clinics in Basel and Bern. Diffuse goiters (parenchymatous and colloid) were more common in Basel than in Bern, while nodular goiters (struma nodosa) were less common in Basel than in Bern. The relation of diffuse goiter in Basel and Bern is 3:2. This difference may be due to the greater number of operations for Basedow's disease in Basel —D M

Traitement THYROÏDIEN de la furunculose Savini (E), Prog Méd (Paris), 1921, 36, 178-179

Having had excellent results with thyroid treatment in a case of furunculosis complicating eczema, Savini systematically treated a series of cases of furunculosis with this drug, giving 2-3 cgm every other day. The results were notably satisfactory. Nineteen males from 16 to 43 years old and eight females, 19 to 32, were

included in the series The results were explained as due to two factors stimulation of the defensive mechanisms and attenuation of the anaphylactic condition created by the infection itself—R G H

Studies of the chemical composition of the THYROID gland Zunz (E), Arch intern de physiol (Paris), 1921, 16, 288-306

This is probably the most extensive tabulation of analyses of the thyroid gland It is shown that the thyroid of man weighs on the average between 26 and 30 gm between the ages of 19 and 55 years The variability, however, is great The H₂O content also varies within relatively wide limits, but approaches a mean of 75% to 76% for all ages in which the weight of the gland does not pass 60 gm The average composition remains relatively constant in the adult in spite of large individual variations observed at all ages There is always found more iodine in the glands obtained from men between 25 and 55 years of age than in glands from men of 19 to 24 years This average content of iodine in the fresh or dry gland tends to increase with the diminution in weight of the thyroid The iodine content averaged 0.56 mgm per gm of fresh substance from 19 to 44 years, it increased gradually from 0.23 mgm in heavy glands to 0.68 mgm in glands of low weight No particular difference in the iodine content of the two lobes was found—Chem Abst, 15, 2116

The excitation of surviving UTERUS and intestine by organ extracts and dialysates (especially those of the UTERUS) [Die Erregung des uberlebenden Uterus und Darmes durch Organextrakte und diolysate (besonders aus dem Uterus)] Backman (E Louis), Arch f d ges Physiol (Berlin), 1921, 189, 261-281

Dialysates of rabbit uterus contain substances which stimulate rabbit intestine The action is not antagonized by atrophine and is only slightly strengthened by acetylising It cannot therefore be due to choline Over 90% of the observed action is due neither to choline nor to serum compounds Similarly dialysates, and also aqueous and alcoholic extracts of cow-uterus excite rabbit and guinea pig uterus and rabbit intestine, and 90% to 96% of the action is due to other substances than choline or blood serum compounds These substances are not destroyed by boiling, are soluble in alcohol, and are not produced by bacterial action nor by autolysis Intestine and muscle extracts yield substances besides choline with similar properties Isolated rabbit and guinea pig uterus show varying sensibility to choline Usually the reaction is much less than that of the intestine Choline therefore is not of importance for automatic uterus movements—A T C

(VAGOTONIA) The pathogenesis of bronchial asthma (La patogenia del asma bronquial) Mora Quimper (A.), Cron Méd (Lima), 1920, 37, 164-170

The investigations of late years concerning the relation of endocrinology and the vegetative nervous system have shown the role that vagotonia plays in such different syndromes as bronchial asthma and spasmodic constipation. The author considers bronchial asthma from this viewpoint and explains it on the basis of the antagonistic action between the vagus and sympathetic fibers.—Author's Abst

VAGOTONIA (*Zur Frage der Vagotomie*) Pophal, Deutsche med Wchnschr (Berlin), 1921, 47, 881

The teachings of Eppinger and Hess prove that the authors do not know the meaning of the word "tonus." Tonus has nothing to do with the nervous system. An absolute antagonism between the sympathetic and parasympathetic systems does not exist. The pharmacological method of Eppinger and Hess, used for the diagnosis of vagotonia, seems to have no value. Frank has stated that perhaps paralysis agitans is a classical vagotonia. He assumes that every muscle has a parasympathetic innervation, but this has never been proven. Frank also believes that perspiring in paralysis agitans is a symptom of vagotonia. This is not true, the sweat glands have, as far as we know, only a sympathetic innervation. The "vagotonia" is a poor hypothesis, built upon unproved statements. (These few lines impress the abstractor as containing more common sense than the complete literature that essays to prove the existence of vagotonia.)—J K

The abstracts in this number have been prepared by the staff assisted by

E L Ross, Chicago

Endocrinology

The Bulletin of the Association for the Study of Internal Secretions

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ADRENAL INSUFFICIENCY FROM THE VIEWPOINT OF THE CLINICIAN *

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When the present journal, ENDOCRINOLOGY, was founded, it was deemed greatly to the interest of the newer branch of Medicine it represents, to insure impartiality in its dealings with all professional questions at issue. Hence the present article on a subject reviewed some months ago by Prof G N Stewart (1) from the standpoint of the physiologist, in which he criticizes clinicians, our French and Italian colleagues in particular, because of their recognition of adrenal insufficiency as a morbid factor in many diseases. May there not be another side to this question?

Stewart's main contention is that the effects of removal of both adrenals in laboratory animals fails to reproduce a well marked syndrome of adrenal deficiency, and, therefore, that physicians are not justified in recognizing such a syndrome. Analysis of his paper suggests, however, that if with us, he worked in the clinical field, his conception of adrenal insufficiency would be different, for he would take cognizance as we

*Part of opening scientific address read before the Endocrinological Society of the City of New York, on January 6th, 1922

do, of various pathological factors which partly explain the variations from the specific symptoms observed in *normal* animals after double adrenal extirpation. Again, he would realize that nothing in the pathological field corresponds with the sudden enucleation of the adrenals with all other organs and tissues in the body in normal health. Even adrenal apoplexy in which death occurs very soon after the onset of the acute symptoms, there exists a concomitant and causative toxemia with lesions in other organs which lead to hemorrhagic destruction of the adrenal tissues, already themselves the seat, in most cases, of organic lesions, cancerous, tuberculous, syphilitic, etc. Irrespective of any such fulminant and comparatively rare termination, the same local lesions, general toxemia, and its complications, hemolysis, autolysis and the active defensive reaction provoked, must be taken into account to interpret correctly the morbid process involved in adrenal insufficiency.

As recently explained by Sargent (2), what he and Bernard meant (1899) by adrenal insufficiency was a complete deficiency of all the functions of the adrenals ("*un déficit total des fonctions surrénales*") including those of both cortex and medulla, after their destruction by local lesions, cancerous, tuberculous, etc. This cannot, however, rightly be termed adrenal insufficiency, but complete adrenal failure—a condition which should provoke in animals and men, and as it does usually, very grave symptoms usually followed by death—unless there exist reserves of adrenin to which I will presently refer.

What I have termed "hypoadrenia" (1907) is a condition, often observed late in acute febrile infections in which a reduction of chromophil or medullary substance has been repeatedly demonstrated at autopsies. It occurs normally in old age, and has been shown histologically to be due to progressive vascular atrophy of the adrenals. It may also occur in infancy at the weaning period, when metabolic torpor fails to sustain organic functions, also after overexertion which likewise coincides with deficiency of the adrenal content in chromophil substance. In all these there exist besides, systemic phenomena due to the pathogenic agent, toxins, endotoxins, wastes, the defensive reaction, lesions in other organs, including the nervous system, etc., which the trained endocrinologist takes into account. Stewart's lack of familiarity with these complicating factors is explained, doubt-

less, by the identity of hypoadiemia as a pathological entity which physiologists never witness. As the great Russian physiologist Pavloff so clearly urged twenty years ago, referring to the discovery of the gastric nerves by physicians "The world of pathological phenomena is nothing but an endless series of the most different and unusual combinations of physiological combinations which never make their appearance in the normal course of life."

Again, clinicians would not endorse Stewart's statement, when referring to Addison's disease, that the majority of clinical writers still suppose that "it is the loss of epinephrin secretion of the medulla which is the important thing, although experimental physiology affords no basis for such a view." No present day clinician worthy of the name would think of "epinephrin secretion" as a sole factor in Addison's disease, being well aware of the fact that both the medulla and cortex may be the seat of lesions. Nor would a competent therapist administer epinephrin in such cases. Either the fresh gland, a glandular extract or the dried gland, all representing the whole gland must be used to expect beneficial results, as shown by a personal study of 120 reported cases. The single case of sudden death in a soldier reported by Boyd (3) is quoted by Stewart as "a safe conclusion that the medulla is not essential to life" because the man's adrenals were almost entirely converted into structureless masses" though he showed no signs of Addison's disease. A clinician would not consider this as a safe conclusion. Nearly two decades ago (4), I submitted ample evidence quite applicable to Boyd's soldier, to the effect that he could readily have fulfilled vicariously his adrenal function with his adrenals "almost entirely" destroyed functionally. Quoting my own words of 1903 "In four rats which survived bilateral adrenalectomy several months Boinet found three or four reddish organs round the kidneys structurally similar to the cortex of adrenals. In the human being accessory suprarenal bodies have been found in the semilunar ganglion and in the midst of the solar plexus by Jaboulay and by Stilling. Gottschalk found accessory adrenals in the infundibulo-pelvic ligament close to one of the ovaries. Wiesel examined fifteen pairs of testicles and epididymes from the newborn and found accessory suprarenal capsules connected with them 23 times. 5 times on each side and

13 times singly The accessory organs had the same structure that the gland usually shows They were usually situated in the connective tissue about the vas deferens, and were surrounded by a mass of blood vessels In older children or adults no fully developed accessory glands were found, but there were remnants in the form of strings and clumps of cells Aichel, on the other hand, emphasizes the importance of organs found by Marchand near the testes in man and in the broad ligaments of woman, which organs are homologous to the suprarenal bodies "

Stewart also contends that if hypoadrenia means a diminished output of epinephrin, "there is not an experimental fact which shows that this would produce any symptoms at all " He bases this conclusion on the fact that his sections of the splanchnic, bilateral adrenal extirpation, etc, in normal animals did not at once bring on hypoadrenia, because they did not and certain animals did not show its symptoms after weeks and even months, hypoadrenia now recognized by thousands of physicians, does not, he concludes, exist—at least as the supposed expression of a diminished epinephrin output

To establish such a conclusion on a sound basis would necessitate knowing just what double adrenalectomy does in animals and what function this operation inhibits or arrests and thus make it possible to explain the character and meaning of the symptoms it provokes Judging, however, from various statements in his paper, Stewart is no better off in this respect than was Swale Vincent (5) five years ago when he wrote "We know nothing of the *functions** of the adrenal body regarded as an organ on its own account "

Such a result after sixty years, the period elapsed since Brown-Séquard began his work upon the physiology of the adrenals, and notwithstanding an enormous amount of labor devoted to these organs by physiologists since, cannot but suggest that they have been all along on misleading paths Is there not a more promising field of research, one in which their labors would prove more fruitful? That such a field has been available for nearly two decades, among the many postulates vouchsafed, now seems certain, judging from the fact that all the data accumulated during that period, physiological, clinical, biochemical, etc, have tended to demonstrate its soundness Even Stew-

*The italics are my own—S

ard and Rogoff have contributed much confirmatory experimental evidence. The nature of this field will develop as we proceed.

Reviewing some of the physiological work on record and also some of his own, Stewart recalls that while removal of both adrenals in laboratory animals, dogs, cats or guinea pigs, is promptly fatal, there are exceptions. Frogs and rats stand out prominently among these. Hibernating frogs, for instance, have survived as long as 13 days and summer frogs 48 hours, while 50 per cent of the rats lived as long as 5 or 6 months. Although such animals might exhibit a normal temperature, appetite and strength similar to those observed in operations not involving the adrenals, the time came when more or less suddenly there appeared anorexia, marked myasthenia and a hypothermia of as many as 18° F, followed by death. Yet, Stewart believes that there is nothing especially pathognomonic in these symptoms, except perhaps the rapid myasthenia.

What is the underlying cause of the prolonged survival of the animals? As to the rats, Stewart grants that the survival of so many of these animals may have been due to the presence of accessory adrenals. We have seen the frequency of such in various parts of the body even in human beings, but rats are well known to be particularly well supplied with these accessory structures, both cortical and medullary. There is an important feature which Stewart has overlooked, however, in his numerous references to Boinet's work. It is the presence of hematoidin crystals in 75 per cent of his 109 rats deprived experimentally of both adrenals. It was found practically everywhere, including the lungs. Two fatal cases of Addison's disease were also found to present this phenomenon. Why should this product of broken down hemoglobin result from destruction, both experimental and pathological, of the adrenals?

Fifteen years ago (6) a study of bronzing led me to the conclusion that this pigmentation was due to an accumulation of adrenal substance similar at least to melanin in the cutaneous epidermal layer, and that hematoidin found broadcast in the tissues was similar to the cutaneous melanin. We know also that the skin of batrachians, which takes part in their respiration, contains fluids which, on exposure to the air, first become brown then black, precisely as is the case in Addison's disease. The melanophores of the horned toad were found by Redfield (7) to

contain a substance similar to adrenin Abel (8) also "found adrenin in relatively enormous quantity in the skin glands of the toad" Again, I had also described the adrienal substance forming part at least of both hematoïdin and melanin as an oxidase (adrenoxidase) Recently, Bittorf (9) also concluded that the bronzing of Addison's disease was due to the formation of an oxidase in the cutaneous epithelium

These few facts, only submitted as mere clues to a possible connection between the adrenin and hemoglobin, would, if true, go far towards explaining the prolongation of life and the non-occurrence of hypoadrenia in animals deprived of both adrenals Thus in the hibernating frogs of Abelous and Langlois to which Stewart refers and in which the post-operative life was 12 to 13 days, the participation of adrenin in the respiratory process and its presence in this animal "in enormous quantity" would supply a residual reserve quite sufficient to explain their prolonged survival, particularly in view of its greatly slowed consumption Indeed, as observed by Pembrey (10), hibernation even in animals gave as low a respiratory quotient as 0.3-0.4

Does, however, adrenin actually take part in tissue respiration? There is no doubt that there is ample room for improvement of our conceptions in this very connection, for as Halliburton states in the last edition of his text-book of physiology (11), "our knowledge of tissue respiration is so scanty that we can say little of its pathological bearing"

That adrenin does take part in pulmonary and tissue respiration by becoming a part of the hemoglobin molecule, I have been urging repeatedly during the last twenty years Having introduced various data on the subject in the presidential address before the 1918 meeting of the Association for the Study of Internal Secretions, and which, therefore, were published in this journal (12), I will submit in the present connection only the complementary data and those strictly necessary to illustrate the present status of the question

As preamble, it may be stated that the respiratory process has been *sub judice* ever since 1856, when Vulpian, and subsequently Paul Bert, Muller and other physiologists found flaws in the diffusion doctrine It failed to account for the disappearance of all the oxygen in the air in the lungs of strangulated animals, also to explain oxygen tensions in the arterial blood

exceeding greatly those in the respiratory tract, etc. Briefly, these and other disturbing factors led Bohr (1891), a Danish physiologist, to urge the need of a substance having greater avidity for oxygen than the blood itself in order to explain the respiratory process. Bohr's view was sustained by several of his colleagues, Haldane, Lorrain Smith, Harley and others. They failed, however, to identify the substance needed.

In 1903 (13) I first published the personal conclusion that it was the adrenal secretion which carried on this function, having been led to it mainly by laboratory studies (1) of the respiratory system in lower animals, including insects, crustaceans, mollusks, fishes, batrachians, etc., ascending the phylogenetic scale to man, (2) of the biochemical reaction of fluids connected with the respiratory process, (3) of the anatomical relations of the organs exposed to external oxygen-containing media, (4) clinical observations, and (5) comprehensive studies of the literature bearing upon these subjects. All these finally pointed to the adrenals, particularly in view of the marked reducing properties of their extracts long emphasized by Vulpian, Cybulski, Langlois, Battelli and others, as the only organs capable of fulfilling the conditions specified by Bohr.

The presence of the colloid hyaline granules which constitute the adrenal secretion in the adrenals themselves and also in their efferent veins, which in turn carry the adrenin-laden blood to the inferior vena cava, is so well established that testimony to this effect is unnecessary. But is it contained in the caval blood and does it reach the heart? Its presence in both is shown by the fact that when this blood contains adrenin in deficient quantity the functions of the heart are depressed, while an excess of adrenin in the same blood increases its tone. Thus, when Stewart and Rogoff (14) compressed the adrenal veins, arrhythmia was caused, this ceased, however, when the veins were released, thus restoring the flow of adrenin to the inferior vena cava and the heart. Again, while the same physiologists (15) noted that section of the splanchnic nerves greatly diminished or abolished the discharge of adrenin, van Anrep (16) found that when these nerves were stimulated, the cardiac tone was increased, and that this failed to occur when both adrenals were extirpated. Fuhner and Starling (17) observed that while asphyxia caused the heart to dilate, the injection of adrenalin caused contraction of the

heart and raised the blood-pressure in the pulmonary artery. Besides observing that clamping of the adrenal veins caused arrhythmia, Stewart and Rogoff (18) found that when the heart became irregular after sufficient doses of strophanthin injections of adrenalin restored the cardiac rhythm.

The next question in order is whether adrenin is actually present in the lungs. Not only is such the case but it seems to facilitate the free circulation of air in the air-cells by causing dilatation of the bronchioles. M. L. Menten (19), for instance, found adrenalin in the venous blood of the pulmonary capillaries. D. E. Jackson (20) observed that adrenalin caused prompt dilatation of the bronchioles when these are contracted independently of any rise of the blood-pressure. W. R. Dixon (21) obtained a similar action of adrenalin in the decerebrated cat, and noted a simultaneous increase of the volume of air entering the lung.

The crucial test, however, is whether adrenin when added to it can actually change venous blood into arterial blood on exposure to the air by causing its hemoglobin to be converted into oxyhemoglobin. Even this feature of the process has proven true. While Kariya and Tanaka (22) found that adrenalin could itself act as does hemoglobin, Menten and Crile (23) observed that blood from the adrenal vein invariably assumed a bright red arterial color in from one to twenty minutes after dilution with salt solution, while blood from other organs treated in the same manner showed no change. Battelli (24), Kraus (25) and others have found adrenalin in the blood, while Mulon (26) found that the red corpuscles also gave the histochemical reactions of adrenalin. Menten (27) also noted that adrenalin added to human venous blood caused an increase in the oxyhemoglobin absorption bands.

Moreover, adrenin gives rise to all the physical phenomena of the respiratory process. It increases the intake of oxygen, the output of carbon dioxide, the volume of air breathed, the respiratory excursions of the lungs, the depth and rate of respiration. Thus, it was found to increase the intake of oxygen and the output of carbon dioxide by Byelaventz (28), while Bernstein and Falta (29) noted that 1 milligram of adrenalin sufficed to do so, and Menten (30) observed that it "does particularly affect the oxygen exchange" in the lung. Tompkins,

Sturgis and Weain (31) found that intramuscular injections of adrenalin caused an increase both in the total gaseous metabolism and the volume of air breathed. Sandiford (32) specifies that all these phenomena were produced in her experiments irrespective of any action on the blood-pressure. The respiratory excursions of the lungs were found by Januscke and Pollak (33) to be increased by doses as small as 1/600 grain (0.0001 Gm.) of adrenalin, while Nice, Rock and Courtright (34) observed that adrenalin increased the depth of respiration whether it raised or lowered the blood-pressure.

Another crucial question is whether adrenin is secreted in sufficient quantity to meet the needs of pulmonary and tissue respiration, i. e., metabolism, in which it necessarily takes part. I attach importance to this factor because it was at one time justly suggested as an obstacle by a physiological friend, whose opinion was based upon the figures of Trendelenburg and Battelli, since shown to be erroneous. Biedl and also Stewart and Rogoff (35) obtained very different results. The latter physiologists state that "the amount of epinephrin spontaneously liberated in cats was found to vary in different experiments within a rather narrow range considering the differences in the conditions, from 0.0008 to 0.0028 mgm. per minute per animal, or from 0.0003 to 0.001 mgm. per minute per kilo of animal." At this rate taking the minimum figure as basis, a man of 65 kilos would receive 2.70 mgm. in his blood in twenty-four hours. This is ample to meet the needs of systemic oxidation, particularly in view (1), of Schafer's observation that fourteen millionths of a gram of the adrenal principle per kilo of animal sufficed to produce maximal effects, and (2), of the fact that the adrenin secreted probably serves only to replace that which is lost or destroyed, many examples of which I have submitted in various writings.

Finally, that adrenin takes part in tissue oxidation, i. e., metabolism, is shown by its influence on the temperature, basal metabolism and urea excretion, while the converse occurs sooner or later, as every one knows, after removal of both adrenals. The evidence to this effect includes such an array of facts contributed by internal medicine, pathology, pharmacology, comparative anatomy, etc., that a mere fraction of this testimony can be submitted here. Briefly, Oliver and Schafer (36), Morel

(37), Lépine (38) found that adrenin caused a rise of temperature, Reicheit (39) observed that this was accompanied by accelerated metabolism. Large adrenal grafts cause a rise of temperature so great as sometimes to cause death, as observed by Courmont (40), Bra (41), and Jaboulay (42). Malignant adrenal tumors, regardless of histological structure, were also found by Israel (43) to run a febrile course independent of any fever-producing complications. Sandiford (44) found that 0.5 c.c. of adrenalin always caused in endocrine sufferers (73 experiments) an increase in the basal metabolism rate. Tompkins, Sturgis and Wearn (45) observed that the rise in respiratory quotient preceded the acceleration of metabolism. Addis, Barnett and Shevky (46) found that adrenalin in not too large or too small doses in rabbits increased the excretion of urea.

Conversely, I may recall that Brown-Séquard and many physiologists since his time, have noted a decline of temperature in animals deprived of their adrenals, a leading symptom also of Addison's disease along with every sign of slowing of the metabolic rate. The basal metabolism of adrenalectomized cats, carefully controlled by Aub, Forman and Bright (47), showed a reduction of 25 per cent, while the same operation in rabbits was found by Bevier and Shevky (48) to cause a depression of the excretion of urea.

I might add that while German reviewers originally, that is to say in 1903 (49) characterized this function as the outstanding feature of my labors on the adrenals, Weil in his recent (1921) book on the endocrines (50), concludes that the suprarenal gland is directly concerned with oxidation.

If facts count at all, the data submitted should suggest that I was not on the wrong path when I wrote in 1903 (51) "1 The adrenals secrete a chromogen—a colloid, hyaline fluid—which leaves the organs through the suprarenal veins, and is mixed with the plasma of the venous blood in the inferior vena cava. 2 When the venous blood reaches the pulmonary alveoli the marked affinity of the adrenaized plasma for oxygen causes it to absorb this gas from the alveolar air. 3 The carbon dioxide in the blood is thus forcibly replaced by oxygen and expelled with corresponding vigor. 4 The red corpuscles, after this operation, bathe in an oxygen-laden medium, and their hemoglobin becomes reconverted into oxyhemoglobin."

The purpose of this evidence being only to point out the vast reserve which a normal animal may possess, I will not introduce the data which point to the role of the red corpuscles in the process—one quite different from that now taught, nor the special role in it of the adrenal medulla. Neither will I review what knowledge we possess of the connection of the cortical portion of the adrenals therewith.

Briefly, in the face of all the above evidence, Stewart's condemnation of hypoadrenia as this syndrome is interpreted by clinicians does not appear justified. His argument based on the survival of experimental animals after removal of both adrenals and the absence of symptoms during that period are invalidated if, in addition to the *numerous accessory or aberrant adrenal tissues in the body*, there exists a *large systemic supply or reserve of adrenin* from which a normal animal deprived of both adrenals can draw for a time, i e., as long as its reserve will last, then show the symptoms of adrenal failure and die. The presence of such a reserve has been indicated by the *widespread distribution of hematoidin and of melanin, both hemoglobin bodies of which adrenin forms part*, after removal of both adrenals in rats and in advanced Addison's disease, and the *connection of adrenin with hemoglobin in the respiratory process*.

The suddenly produced morbid process which double removal of the adrenals entails differs entirely, we have seen, from that recognized as hypoadrenia by clinicians. For them hypoadrenia means a gradual failure of the adrenals, which renders these organs unable to supply the body at large the stock of adrenin it needs to carry on, from my viewpoint, its respiratory functions, i e., tissue oxidation. Whether due to local lesions, or to conditions such as an acute febrile process, which drain the reserve beyond the restitutive efficiency of the adrenals, the result is the same: there comes a time when in addition to symptom complex of the causative disease, there appear certain specific symptoms which are those of gradual adrenal failure. Now what are these symptoms? They are precisely those observed in animals deprived of both adrenals, when the function I have attributed to the latter, tissue oxidation, is taken into account, to-wit anorexia, muscular weakness progressing to paralysis, loss of tension of the eyeballs, gradual fall of the

blood-pressure and steady fall of the temperature until death ensues

It would take too much space to adduce all the evidence available, but what I have submitted should suffice to indicate that physicians who have observed and described hypoadrenia in its various forms were justified in doing so. Referring only to adrenopathies, Pende had good ground for his acceptance "of the hypoadrenal constitution as a clinical and pathological entity." The group of cardiopathies of the hypoadrenal type observed in soldiers described by Satre is also a defensible entity, a statement which applies as well to the sudden deaths from adrenal asystole described by Josué. The syndrome of hypoadrenia observed in soldiers suffering from infectious icterus, dysentery, typhoid, excessive fatigue, etc., is equally justified. I have myself observed and studied the majority of these pathological states, and there is no doubt that with the adrenals interpreted as participants in pulmonary and tissue respiration, appropriate replacement organotherapy, adrenalin mainly (using the suprarenal gland in chronic conditions such as Addison's disease), is a life-saving measure often so marked as to suggest undoubted resuscitation.

It was I, moreover, who called attention in 1903 to the fact that Asiatic cholera was "in reality the gravest form of adrenal insufficiency" with "marked muscular weakness," "pulse rapid and weak, sometimes intermittent," "temperature in mouth and surface very low," "respiration frequent and difficult and cyanosis"—all typical signs of adrenal failure similar to those observed when after the period of survival after removal of both adrenals an animal approaches the moribund state. The endotoxins of the cholera vibrio were since found by Déméstreescu (52) to cause disappearance of chromophil reaction of the adrenals. Confirming my views, Drake-Brockmann (1910), Plovesana (1912), Namé (1914) used adrenalin and noted a remarkable tolerance, while its efficiency was striking.

Stewart might urge in this connection that "there is nothing specially pathognomonic in such symptoms unless indeed it be the muscular weakness which may seem to come on with more rapidity, etc." Yet, the fact that he cannot himself explain their origin with all experimental data at his disposal is suggestive. Nor can anybody, in my opinion, do so *without*

taking the role of adrenin in tissue oxidation into account It is the key to the whole situation and with scientific accuracy explains the syndromes of both the adrenal insufficiency due to complete destruction of the adrenals, as it is interpreted by Sergeant, and hypoadrenia as it is interpreted by myself, a larval form devoid of permanent invalidating lesions, which may be produced by many pathogenic conditions, and the non-recognition of which would be a calamity to a large proportion of the sufferers entrusted to our care

Stewart refers to "exact physiological science" as the basis of his criticisms of clinicians' conclusions The foregoing analysis indicates, if I am not mistaken, that while of incalculable value in its own legitimate field, physiology does not convey the truth when it undertakes alone to analyze pathological phenomena When a pathological state is produced in a normal animal by physiological methods, *it portrays only what the same methods would provoke in man*, and even then allowances would have to be made As a standard for pathological states which necessarily introduce many fundamental deviations from the normal, however, experimental physiology in *normal* animals tends to mislead Indeed, as in the case of suprarenal insufficiency or hypoadrenia, it may prove costly in human lives—a fact which should inspire great reserve in the presence of therapeutic results attained, even though they disagree with experimental observations which at best, judging from the fate of the theories of Oliver and Schafer, Abelous and Langlois, Cannon and other physiologists of the first order, cannot but offer a frail foundation for a final judgment Meltzer has wisely condemned experimental control over measures found useful

An experience of over forty years as a physiologist (my first chair), clinician, encyclopedist and editor, has only served to emphasize the fact that physiology will become a "great white light" when physiologists will fully realize that its true worth lies in *constructive synthesis* along with contributions from all other branches of medical science Hence the fact that even the comparatively few data submitted in the foregoing pages in support of the respiratory doctrine, include contributions from several subdivisions of medical knowledge, clinical medicine, physiology, pathology, pharmacology, biological chemistry, zoology, etc These are not used in the manner sometimes ob-

served in comprehensive works, where each branch is tersely reviewed separately, but they are made, instead, to participate in the upbuilding of each subdivision of the subject studied, thus forming in the end (the conclusion or postulate reached) a mosaic, as it were, of all knowledge available on the subject. Apparently discordant data, always considered with due respect, often prove not to be such, for, if based on sound observation, they usually find in the other branches of knowledge one or more links which convert them into valuable assets. As examples, I might mention the "obsolete" tonus theory of Oliver and Schafer, the "obsolete" antitoxic theory of Abelous and Langlois, and the much questioned emergency theory of Cannon, which though severely assailed by physiologists, are to me brilliant and invulnerable contributions to our knowledge when regarded as manifestations of the function I have attributed to the adrenals, and when they are elucidated by the many sidelights it affords.

It is because I have followed this plan, which does justice to all sincere workers, that my interpretations of the main endocrines, even though seemingly anomalous at first, have, as we have seen in the case of the adrenals, been sustained by experimental and clinical evidence from all directions. No one today would dare to state that we have reached beyond the threshold of endocrinological knowledge, but it is essential for the welfare of suffering mankind, the clinician's main concern, that even the threshold be that of the right door.

In closing, I cannot but emphasize anew what I have long urged. This is that the *harmonious cooperation of all medical scientists*, each branch being regarded as a spoke in the wheel of progress, will in the end prove to be the best policy. In no field of human endeavor is this attitude more needed today than in endocrinology.

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THE INFLUENCE OF THE ENDOCRINE SYSTEM ON INTRAOCULAR TENSION

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This report comprises a short summary of my clinical observations as regards the relation between intraocular tension and the internal secretions. The way such a relationship was suggested has been already published (1, 2). This report is presented in the hope that it will lead others to extend the observations in cases of different dysfunctions of the various endocrine glands.

The current theories which seek to explain the regulation of intraocular tension are more or less inadequate to account for our clinical experiences. Even those based on blood pressure are unsatisfactory, because we find that (1) the tension of normal eyes can change without change of the blood pressure, (2) there are cases in which the eyes of young individuals with relatively high blood pressure show a lasting hypotension, (3) we find sometimes in case of normal eyes a remarkably high tension, although the blood pressure is normal or even lower than the average for the given age.

These facts interested me particularly because I have made systematic studies with the tonometer of Schiotz since 1910 (3) and was led to the conclusion that the long discussed problem of glaucoma will not be solved either by anatomical studies alone or by studies of the blood pressure and changes in the intraocular blood vessels. We have reason to believe that acute inflammatory glaucoma as well as so-called simple glaucoma is only a manifestation of certain constitutional abnormalities. I should like to go a step further and say that even those anatomical anomalies predisposing to glaucoma could be looked upon as probable consequences of certain constitutional anomalies. This conclusion is suggested by knowledge of certain families, several members of which have an unusually great degree of hypermetropia, small eyeballs with relatively large lenses, etc.

Three years ago quite an unusual case was observed in my eye clinic in Pozsony, Pressburg,* which afforded a hint to go farther in studies along this line. The patient was a pregnant woman who showed signs of osteomalacia. Her eyeballs lost their original form, the cornea of both eyes was wrinkled and the eyeballs were so soft that the simple cohesion between the conjunctiva tarsi and bulbi was enough to lead to a deep wrinkle on the upper part of the sclera when the lower lid was pulled down.

The normal intraocular tension is between 15 and 26 mm Hg pressure and when the heart stops beating it sinks to 8 mm Hg. In this case the intraocular tension was less than that of a cadaver, it being even less than 5 mm Hg. I searched for the explanation and what first set me to thinking was a coincidence of pregnancy and osteomalacia. I reflected that either of these conditions may lead to some degree of subtenion and the two together all the more.

This conception led to a systematic examination of the eye tension of pregnant women. We found that among 50 subjects there were 42 with decidedly subnormal tension, two with normal and six with high tension. Those who had hypotension of the eyes showed the signs of pregnancy in the face, hands, skin, etc. These signs are regarded as due principally to hyperpituitarism, which is more or less pronounced in case of pregnancy (Erdheim and Stumme). The average tension of the 42 pregnant women was 12 mm Hg, i. e., much less than the average normal eye tension, which is 20 mm Hg.

Those who had hypertension—and one had even 31 mm Hg pressure, although the eyes were clinically normal—looked unusually fresh in spite of their pregnancy and the facial signs of pregnancy in the lines and color were totally absent. It may be supposed that in these cases the ordinary hyperfunction of the hypophysis was not present.

In the meantime, we had opportunity to examine a patient who had atrophy of the optic nerves, bitemporal hemianopsia, cessation of menstruation and enlarged sella turcica as shown by radioscopy. The intraocular tension in this case was 11 mm Hg.

*The Elisabeth State University originally was located there. In the summer of 1919 the Czech government compelled us to leave it. Since then the work is carried on in Budapest.

in the right eye and 12 mm in the left. A second and a third case of hypophysis tumor showed similar hypotension.

One patient showed typical signs of acromegaly, but for a considerable time had been under x-ray treatment and for several months had received thyroid tablets, the pathological process had been arrested as shown by the fact that for two years the measurements of the bones, extremities, etc., had not changed. In this case visual acuity as well as the field of vision was the same as two years before, the tension was perfectly normal. This spoke for the fact that the balance of the endocrine system had been restored. This observation offers hope that we shall be able to use these ocular tension examinations to decide whether in certain cases treatment has had a satisfactory effect.

This supposition seems to be strengthened by a few cases of osteomalacia. Two cases which were not treated before the examination of the tension took place, had very decidedly low eye tension (the one 12 and 13 mm Hg, the other less than 5 mm). Of the three patients which were operated upon (castration) before we examined their tension, one failed to show any conspicuous improvement of the clinical symptoms, she could not stand on her feet and had as much pain as before the operation. This patient had subtension (12 mm) in both eyes. The other two, who got decidedly better, had normal tension. The only remarkable circumstance was the great difference of the tension between the right and left eyes. The rule is that both normal eyes in any given subject have the same tension. The tension in one of these cases was 23 mm Hg in the right and 15 mm in the left eye, in the other case it was 18 mm in the right and 15 mm in the left eye.

The only previous publication which gave a hint that abnormal eye tension may be connected with dysfunction of certain endocrine glands was that of Hippel (4), who found that patients with glaucoma gave a positive Abderhalden reaction with thyroid and thymus. Although these findings did not induce many investigators to extend the studies, they deserve the greatest attention.

Later on, Hertel (5) found that patients with hyperfunction of the thyroid have low intraocular tension and patients with glaucoma have signs of hypofunction of the thyroid. Wessely

(6) affirmed that the eye tension of patients with Graves' disease is in most cases lower than normal

My experience does not confirm this. I have found among patients with Graves' disease more who had high tension than low tension, several with decidedly low tension were seen, however. In the older literature we find several articles with the statement that in Graves' disease the high tension of the eye is not a rare exception. Braley and Eyre (7) several times found deep excavation and high intraocular tension in such cases. They, however, did not use a tonometer, but judged by touch only. Gail (8), too, in one case of Graves' disease, found high tension and deep excavation of the optic nerve. In Hippel's article we find a case of Graves' disease ("forme fruste") connected with glaucoma simplex.

It would seem unsafe, therefore, to accept as generally true the statement regarding the low tension in Graves' disease. This apparent contradiction in the results of our examinations is easy to understand if we consider the great variability of the symptoms of this illness. In my experience Graves' disease can cause either type of abnormal eye tension. But in either case we find almost regularly a remarkable difference of tension between the right and the left eyes, and a pronounced *lability* of the tension even during the measurement. This proves that the regulation of the tension is disturbed.

SUMMARY

We find that a disturbance in the balance of the endocrine system causes a disturbance in the intraocular tension. When the balance is restored the intraocular tension approaches or becomes normal. Therefore we may conclude that the hitherto unsettled question of the regulation of the intraocular tension depends primarily on the function of the endocrine glands. Although the disturbed function of one gland of this system provokes a change in the function of others and, therefore, we usually have to do with a pluriglandular disturbance, the glands that seem to play the principal role in the regulation are the hypophysis, thyroid, thymus and gonads.

Determining of the lasting changes in the intraocular tension may give us important hints and may be used as a valuable diagnostic help when we suspect some disturbance of the endo-

crine system or in the function of one certain gland. We recommend, therefore, the careful and systematic measuring of the eye tension with the tonometer as a diagnostic and in some cases prognostic auxiliary method.

Further observations and therapeutic findings, which are purely of ophthalmological interest, will be published in special ophthalmological journals.

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A CASE OF RETARDED MENTALITY IN A CHILD, TREATED BY ORGANOTHERAPY

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Inasmuch as endocrinology is relatively a new branch of medicine, and the knowledge of the ductless glands and of the influence they exert upon the living organism is yet in its infancy, it is the view of the writer that clinical data are at least as valuable as data obtained in laboratories from observations upon animals. This may serve as justification for publishing the following case.

This is the case of A. F., a girl of 14, of healthy parents and whose birth was normal. When a year old she had convulsions, that came on an average of twice a year until she reached the age of six. Then the convulsions ceased. Measles and tonsillitis were the only diseases the child had gone through. Though her physical development up to about two years ago was apparently normal, her mental development caused her parents considerable anxiety. It took her eight years to complete the first five grades of school, she being obliged to remain two years in each of the last three grades. A tonsillectomy and adenectomy was performed with the view of raising her intellect, but without any perceptible effect on the patient. Her growth during the last two years was suddenly very rapid, and she became tall and lank, but her mental capacities either remained stationary or developed very slowly. She lacked concentration—she often returned her library books without reading them. Broken dishes and faulty chores were frequently the despair of her parents.

With such a history this girl came under my observation on Sept. 27, 1920. The following data were obtained. The girl was tall for her age and weight, measuring 62 inches in height and weighing 86.5 pounds. She had long arms, large hands, long fingers, long legs and large feet. Otherwise physical examination was negative. Her mentality corresponded approximately to that of ten years. At the time of my first examination the patient was in the fifth grade, this being

her second year in the same grade The patient was given capsules three times a day, containing the following formula

Pituitary Gland (anterior lobe)	gr 11
Thymus gland	gr 1
Thyroid gland	gr 1/12
Calcium Phosphor Comp q s ad	gr v

With the exception of two months, March and April, 1921, the patient was taking these capsules regularly from October, 1920, to July, 1921 In March and April she ceased to take them because her brothers teased her, implying that her "wisdom" and smartness came from these capsules

5 (1921) Last Name <i>Y</i>		First Name and Initial <i>P</i>		BOSTON PUBLIC SCHOOLS PUPIL'S REPORT CARD																
				Grade <i>2</i>		Room <i>14</i>														
SCHOOL YEAR	Number of Sessions Absent	Number of Times Tardy	Conduct	Effort	Reading and Literature	English	Spelling	Pennmanship	Grammar	Arithmetic	Geography	History and Civics	Music	Drawing	Mental, Physical or Domestic Arts	Physiology and Hygiene	Science	Physical Training		
191	Ab.	T	C	Eff.	Eng.	E	Sp.	Pe.	Gr.	Ar.	Ge.	H. & C.	M	D	M	P	D. & H.	Sc.	P. T.	
Sept. & Oct.				3	2	3	2	2		2	5		1	2	3			1		
Nov. & Dec.				1	1	3	2	2		2	1		1	2	3	2		1		
Jan. & Feb.				1	1	2	2	1	2	2	3		1	2		1		1		
Mar. & Apr.				2	3	2	2	1	3	4	4		1	3		1		2	2	FE
May & June				1	1	3	3	1	3	5	3		1	3		1		1		

"THE HOME AND THE SCHOOL SHOULD WORK TOGETHER FOR THE GOOD OF THE CHILD"

It is important that the teacher should be fully informed as to the child's physical condition life outside of school, and previous history Parents are cordially invited to confer with the teacher or the principal

School

Signature of Teacher

Garrison

Marguerite Rich

Library Bureau 647410

With this in view, it is interesting to study the reproduction of the original school card, where her school work was marked bi-monthly It is seen from this card that her November and December record was a great improvement over the one of September and October, while the January and February record shows a still further advancement The March and April record is quite in accord with the omission of the capsules during these months, while the resumption of these capsules during the months of May and June resulted again in a considerably improved school record

On Feb 11, 1921, her height was 63 5 in , her weight was 92 lbs , her span (from middle finger to middle finger), 63 5 in , her pulse, 80 , blood pressure, 60-100, secondary sex characteristics (enlargement of the breasts, growth of pubic and axillary hair) present

On Nov 6, 1921, the following data were obtained Height, 64 in , weight, 98½ lbs , span, 64 in , blood pressure, 50-110, pulse, 80 Her first and only menstruation occurred two months ago

COMMENT

The history of the case—convulsions during the first six years, the sudden growth in the last two years, the present stature, the span being equal to or even exceeding the height, the backwardness—all this points to a so-called mild form of gigantism, a condition that is supposed to result in growing children from an abnormal activity of the anterior lobe of the pituitary gland. It is the same process that brings about the characteristic symptoms of acromegaly in adults. The supposed abnormality of the anterior lobe called in my formula for two grains of anterior lobe pituitary, the small dose of thyroid being added on the principle that the latter is a strong synergist with the former, the thymus gland was also added because of its supposed influence upon the skeletal growth of the child, and finally the salts were added as a hematic.

The writer is fully aware of the warning given by Cushing (1), Hoskins (2), and others, of the danger of overestimating the efficacy of organotherapy. Granting the timeliness of this warning, we must not go too far in the opposite direction and underestimate the importance of clinical observations carefully and conscientiously made. We must not forget that, after all, the experimental observations in the laboratories must be first translated into clinical observations before their full significance and importance is made clear.

SUMMARY

The case is described of a girl 14 years of age who had manifested rapidity of growth and developed skeletal proportions suggestive of gigantism. Considerable mental retardation was evidenced. Obvious improvement in her scholastic record was seen while she was undergoing organotherapeutic treatment. Renewed retardation occurred when treatment was discontinued and there was improvement with its resumption.

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STUDIES OF THE THYROID APPARATUS V
THE SIGNIFICANCE OF THE COMPARATIVE MORTAL-
ITY RATES OF PARATHYROIDECTOMIZED WILD
NORWAY RATS AND EXCITABLE AND
NON-EXCITABLE ALBINO RATS

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PHILADELPHIA

In the first paper of this series (1) a report was made of a comparative study of the mortality rate of two groups of parathyroidectomized albino rats. Although the members of both groups were descendants of the same parent stock they differed in the general trend of their excitability or readiness to respond to exogenous stimuli and consequently in their muscle tone. The one group, called the "Stock Albinos," presented the normal picture of low threshold of response to stimulation and high muscle tone. These rats were easily excited. The mortality rate within 48 hours after parathyroidectomy was 79 per cent and was accompanied by *tetania parathyreopriva*. In the other group, designated as the "Gentled Albinos," in which excitability and muscle tone had been reduced to a low level by constant handling and petting, the mortality rate was but 13 per cent.

As a result of these observations the hypothesis was advanced that the occurrence or non-occurrence of early death from the loss of the parathyroid glands depended in large part on the general trend of the reactions of the organism to exogenous stimuli. These reactions were considered as being mediated by the relative degree of control of the animal by the instincts of flight and pugnacity as manifested in their affective aspects of fear and anger. In these reactions the nervous system is obviously the directive mechanism. Consequently the stability of the nervous system was considered as a factor of importance in the resistance of the albino rat to the loss of the parathyroid secretion.

On the basis of this hypothesis it seemed desirable to determine the mortality rate of the untamed wild Norway rat caged

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for one or two generations. This animal gives the impression of a very excitable organism in which the instinct of pugnacity is apparently more highly developed than in the "Stock Albinos."

The Norways used in this series were kindly furnished by Doctor Helen D. King from her stock and were of the F_2 generation. Rats of both sexes and of different ages were used. The sex and age distribution approximated that of the earlier study. The conditions of diet and caging were likewise the same. Inasmuch as this investigation was confined to the determination of the mortality rate due to the loss of the parathyroid secretion, and since it had been previously found that identical mortality rates obtained whether parathyroidectomy or thyro-parathyroidectomy was done, the latter operation was done on the majority of rats at this time for purposes of convenience. As in the first study, 48 hours from the time of operation was taken as the standard of survival.

A total of 102 rats was used. Of this number 92 died within the stated period. All of the rats save three showed tetany. The mortality rate of the wild Norway rat due to the loss of the parathyroids is thus 90 per cent. This rate is higher than that for the excitable "Stock Albinos," a result which was to be expected and supports the original hypothesis. A comparison of the mortality rates of the three groups is given in the accompanying chart.

The difference between the two excitable groups is actually greater than the relative values indicate because of the fact that most of the survivors of the 48 hour period of the Norways died within two or three weeks after the operation, while most of the survivors of the "Stock Albino" group lived until killed for other purposes (for two or three months).

The interpretation of these differences on the basis of the stability of the nervous system is further supported by the fact that when a litter of eight pure black rats 75 days old, which are normally as excitable as the wild Norway, was parathyroidectomized all but two survived the 48 hour period. These rats had been tamed to the point where they gave but little evidence of fear or anger and where the muscle tension on handling was

obviously of a low order. All other conditions such as diet and caging were the same as for the other groups.

On the basis of these results it is possible to explain the differences in the observations of other investigators on the survival or non-survival of the rat from the loss of the parathyroid secretion. Cristiani (2), Erdheim (3) and Isehn (4) found a high mortality rate after this operation. Vincent and Jolly (5), Fainer and Klinge (6) and others report the contrary. The

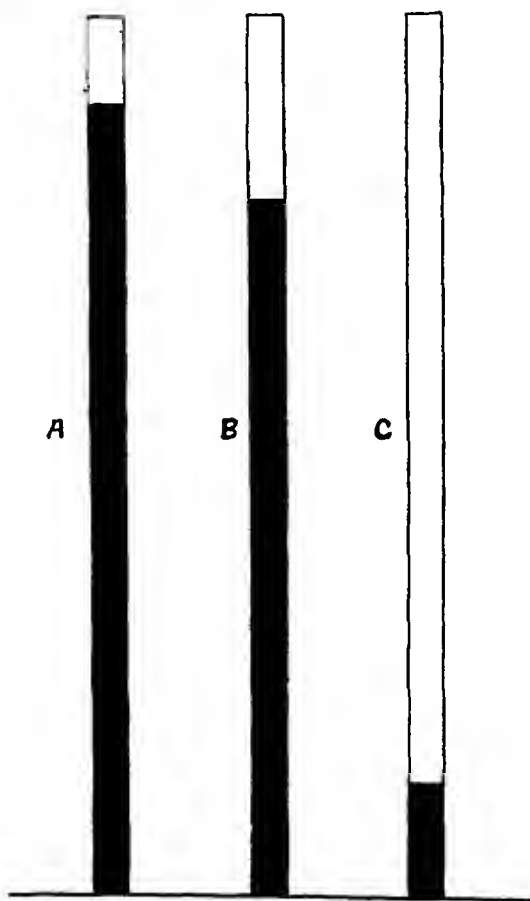


Diagram showing relative mortality after parathyroid extirpation in wild Norway (A), untamed Albino (B), and gentle Albino rats (C)

latter also failed to obtain tetany after parathyroidectomy of five adult wild Norway rats caught in the open and of unknown age. On the other hand, I removed the parathyroids from three Norways over two years old. They all showed tetany and two

died within 24 hours Farner and Klinger attribute the low mortality following parathyroidectomy in their rats as compared with the high values found by other observers to differences in the strains used While this may be a factor, I believe that the differences are due to differences in the intensity of the neural reactions of the various groups in the response to external stimuli as largely directed by the degree of control of the organism by the instincts of flight and pugnacity That the emotional trend of the individual is an important factor in the degree of resistance to disturbing conditions is well shown from the clinical experiences of Cile (7) This investigator believes that the preliminary stabilization of the patient with the view to removing fear of operation and the consequent lessening of neural tension is an important prerequisite to surgical success His results are a strong support for this belief It cannot be doubted that not only does the bodily constitution affect the functioning of the nervous system, but also that the neural activities have a profound effect upon bodily constitution This I have discussed in some detail elsewhere (8)

The objection may be raised that those rats which survive the extirpation of the parathyroids do so because all the parathyroid tissue has not been removed,—that is to say that in the survivors either accessory or aberrant parathyroid tissue is present Erdheim (3) and Farner and Klinger (6) have made serial sections of the neck and thymus of rats and report the finding of minute groups of cells simulating parathyroid tissue Nevertheless they state and apparently believe that this so-called parathyroid tissue can have no important physiological function Thompson (9) from a similar study comes to the conclusion that the rat has but two functioning parathyroids It is nevertheless true that there may be occasionally an animal in which a parathyroid may be found aberrant Farner and Klinger report some 12 per cent of this type From their brief description, however, it is evident that by far the greater number of these aberrant parathyroids are easily recognizable I, too, have occasionally found a parathyroid lying adjacent to the thyroid instead of embedded in this tissue as is usual The percentage of undetectable aberrant parathyroids is very small and can play no significant role in the causation of the wide dif-

ferences observed in the mortality rates of excitable and gentled rats. Moreover, those rats which survive the parathyroidectomy may still show tetany, and disturbances of growth of the incisors occur with remarkable uniformity. Although it is impossible to say definitely that there is no functioning parathyroid tissue in those rats which have survived the removal of the parathyroids from their usual location, yet since only those rats were included in this study from which two well recognized parathyroids were taken, and in view of the facts presented above, the conclusion is justified that the differences between the three groups studied are valid evidence of differences in the respective resistances to the loss of the parathyroid secretion.

This idea serves as a working hypothesis as the following discussion will show.

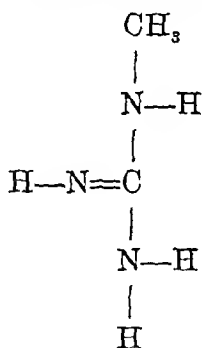
There are at present three theories as to the cause of the tetany occurring in animals following parathyroidectomy. There is the theory of a calcium deficiency in the blood which was developed by MacCallum and Voegtlin (10). This calcium deficiency results in a disturbance of the ion equilibrium of the blood and a resultant increase in nerve irritability. There is the theory advanced by Wilson, Sterns and Janney (11) in which the tetany is considered as a sequence of a disturbance of the acid-base equilibrium of the blood. The observations in support of this idea are as yet too few and too incomplete to justify its acceptance. Moreover, neither Hastings and Murray (12) nor Underhill and Nellans (13) by modern methods have been able to support the observations of the proponents of this theory, while Greenwald (14) presents evidence that the increase in the sodium ion is a contributing factor rather than the so-called alkalosis. Finally there is the theory of Paton and Findlay (15) that the tetany is a result of a toxemia due to the presence of a guanidine compound resulting from protein catabolism.

The observations reported in this and previous papers (1) (16) fit in with this last theory.

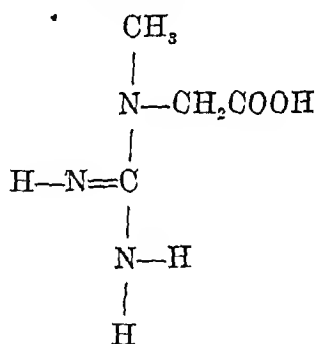
If we assume that a function of the parathyroids is to provide a means to the organism of facilitating the disposal in some way or other of the toxic compound guanidine or methylguanidine there is a considerable body of data in support of our hypothesis. For Koch (17) has found that methyl-guanidine

is excreted in parathyroid tetany. This has been confirmed by Burns and Sharpe (18), who also found that methyl-guanidine occurred in increased amounts in the blood of animals in this condition. Recently Nattrass and Sharpe (19) have found that in adolescent tetany there is a marked guanidine excretion. The objection has been raised that the method of determination of methyl-guanidine would tend to change creatine present into that compound in view of the alkalinity of the solutions used. I have found no evidence whatsoever of any decrease in the total creatinine of muscle extracts when incubated for 24 hours at body temperature in alkaline solution (20). Paton and his co-workers and others have found that methyl-guanidine increases nerve irritability. Methyl-guanidine is de-acetylated creatine as the formulas show.

Methyl-guanidine



Creatine



Pekelharing and Van Hoogenhuyze (21) have pointed out the relation between muscle tone and creatine and their general conclusions are supported by the studies of Leathes and Orr (22) and Hammett (23). It appears as if the degree of creatine formation is directly related to the degree of muscle tone. Now if guanidine, or methyl-guanidine, is a normal by-product of that phase of muscle metabolism concerned in muscle tone, then when the parathyroids are removed, and there is removed with them the chief agency for detoxicating the guanidine compound, possibly by assisting in its transformation to creatine as has been suggested by Henderson (24), we should expect to get the evidence of the greater or acute toxemia in those animals in which excitability and its consequent high neural and muscle tension are present, and the lower or chronic toxemia in the gentled

animals where the muscle tone is low because of the high threshold of the nervous system to exogenous stimulation. Such we have seen to be the case -

I would not for one moment be taken as denying the occurrence of a decrease in the blood calcium and a possible disturbance of the ion and acid-base equilibrium, or that these changes may participate in the ultimate outcome. That such disturbances occur in infantile tetany has been demonstrated recently by Tisdell, Kramer and Howland (25), who found that although the calcium concentration of the blood is markedly diminished the amounts of sodium present remain the same. *But these are secondary phenomena.* The relative lapse of time between parathyroidectomy and the appearance of tetany and disturbed acid-base or calcium equilibrium afford no support for the former theories. In fact, it is difficult to believe that the parathyroids are the direct regulators of the sodium-calcium ratio, the ionic equilibrium and the acid base balance of the body. From the available data it is more reasonable to believe that when the parathyroids are removed the organism loses in great part its capacity to get rid of the toxic nerve irritant, guanidine or methyl-guanidine, a product arising largely from the metabolism of the condition known as muscle tone. There is then set up a condition of heightened neural activity. This results, among other things, in a disturbance of muscular activity. As is well known, this leads to marked changes in the respiratory exchange. From this arise changes in the composition of the blood. Thus the ion equilibrium is upset and the various recorded changes occur. That the parathyroids do play some part in the creatine metabolism I have recently shown (16). Their exact role has yet to be determined.

This then is our working hypothesis

From the observations on the three groups of rats certain general conclusions of practical significance can be drawn. It is evident that the more excitable the organism the higher is the neural and muscular tension, the greater is the instability, the greater is the production of toxic by-products, the greater is the need for the mechanism for getting rid of these poisonous substances and the greater is the dependence of the organism

on the parathyroids in averting disturbances arising from these sources

The protective function of the parathyroids apparently is of decreasing importance as the tendency for acceptance of environmental changes without protesting response is increased. The result of the diminution of the domination of the emotions of fear and anger, which as Stanley Hall (25) points out is a major impelling motive of man, is a lessening of the production of organic changes which are detrimental to the individual. Resistance is raised. It would appear as if Cline, in his custom of having his patients undergo a preliminary period before operation in which they are familiarized with the procedure of anesthesia and in which by education fear is lessened, has been putting into practical use the principles which these experiments on excitable and gentled albino rats seem to establish.

SUMMARY

The mortality from parathyroid extirpation in wild Norway rats was found to be 92 out of 102 subjects, or 90 per cent. In case of gentle albino rats the mortality had previously been shown to be 13 per cent and of untamed albino rats, 79 per cent. The high mortality is regarded as correlated with heightened neuro-muscular activity and resultant augmented toxin formation. The bearing of these findings on certain clinical observations is discussed.

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THE USE OF PITUITARY EXTRACTS BY MOUTH IN THE TREATMENT OF DIABETES INSIPIDUS

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It has been quite conclusively shown that pituitary extract—posterior lobe—is effective in controlling the polydipsia and polyuria of diabetes insipidus. It has, however, been necessary in practically every case to administer the extract by intramuscular injection. As a rule one injection per day, regardless of the size of the dose, is not sufficient to relieve the patient. Usually two or three injections of 1 cc each are required to keep down both the day and the night intake and output. Since, in most cases, this treatment has to be continued indefinitely a great financial and physical burden must be endured by the patient. The present price of the liquid extract is about 25 cents per 1 cc ampoule. Since it usually requires three injections per day the cost to the patient would be \$0.75 per day for the extract, alone. To this is to be added the physician's charge for giving the injections, therefore, the cost to the patient could not be less than \$1.50 per day. Of still greater importance is the patients' loss in time in being required to make three visits per day at the physician's office.

On looking through the literature we find that in practically every reported case of diabetes insipidus the administration of pituitary extracts by mouth has been tried and reported as a failure. In a few cases the feeding of four to seven whole beef glands has been reported as successfully reducing the polyuria during the night.

In the treatment of the following case it was our purpose to find, if possible, a successful method of giving pituitary extract by mouth. Since there is a strong probability that the effective agent of the extract is destroyed in the stomach, we sought to overcome this possible difficulty by giving the extract in salol coated capsules. The preparation used was the desiccated posterior lobe as prepared by Armour & Co.

The price of the desiccated posterior lobe extract (Armour & Co) is about \$2 00 per dram This would make the capsules (2 gr) cost at the rate of fifteen for \$1 00 The salol coating would increase this cost slightly At the rate of four capsules per day the cost to the patient would be \$0 35 to \$0 50 per day, about one-third the cost of the injections The great saving to the patient in time and money is quite evident

CASE HISTORY

Case B V—The patient was a white male, age 37, by occupation a railroad brakeman

His weight at the onset of the present illness was 145 pounds, on admission to the hospital it was 165 pounds, six months after admission to hospital it was 195 pounds

He was well nourished and well developed, and did not appear to be sick

He entered Barnes Hospital on March 31, 1921, with the complaint of excessive thirst, frequency of urination, diarrhea and almost constant headache

His family history was unimportant

His past history indicated the usual childhood diseases He had paralysis of right side of face and bilateral impairment of hearing twelve years ago

Gonorrhea and chancroid, contracted fourteen years ago, received no treatment

Nine years ago he was troubled with weakness, shortness of breath and nervousness He lost 30 pounds of weight in one year He consulted a physician at this time and was told that he had pulmonary tuberculosis and that he could not live over one and one-half years At this time the patient began excessive indulgence in alcohol This excessive drinking was continued for several years

The patient was married nine years ago and has two children living and well There is a history of one miscarriage

His present illness began two years ago and the trouble came on quite rapidly He first noticed that he was drinking large amounts of water and that he had to get up several times at night to urinate

Within a month after the patient first noticed his increased thirst and frequency he was voiding large quantities of clear urine about every thirty minutes day and night He states that on several occasions he measured his urinary output for twenty-four hours and found it to be twenty to twenty-five quarts

From the beginning of his present trouble the patient has had more or less constant headache He also complains of dizziness and of being easily fatigued He thinks that his memory is impaired, and states that his head "feels dead"

Since the onset of the trouble he has had four or five loose stools per day. His appetite has always been good.

Since one or two months after the onset, the patient's condition has remained quite constant until he entered Barnes Hospital.

Physical examination gave no definite pathological findings.

Neurological examination showed a seemingly normal mental condition. Judgment and memory were good. There were no speech defects, nor pathological reflexes.

Laboratory and special examination showed normal blood findings. The urine showed a very low (1001-1002) specific gravity on admission, the total solids for twenty-four hours were within normal limits.

The blood Wassermann reaction (four taken) was negative.

One cerebro-spinal fluid Wassermann was taken with negative results.

The phenosulphonphthalin test for kidney function showed a return of 75 per cent of the dye in two hours.

Ophthalmoscopic examination showed that the discs were normal.

The visual fields were normal.

Stereoscopic plates of the skull showed no definite abnormalities.

A gastric fractional analysis showed a normal acidity curve.

A gastro-intestinal fluoroscopic examination showed a marked hypermotility of the whole tract.

The blood pressure on admission was 110/65, after treatment it was 125/70.

Progress in the Hospital When the patient was first admitted to our service his twenty-four hour fluid intake and output ranged between twelve to fifteen liters.

In order that we might secure a more stable intake and output we first had the patient control his intake at a point where he could remain for some time with reasonable comfort. This point was found to be about seven liters per twenty-four hours. After thus limiting the intake for three days the urinary output decreased in proportion and the specific gravity went up to 1011. The patient was now asked still further to reduce his intake. This he did, getting it down, with some difficulty, to slightly less than four liters. The specific gravity went as high as 1013. While on this decreased intake the patient complained of nervousness, dull headache, and sleeplessness.

After keeping the patient on a four liter intake for six days he was put on placebo treatment for four days. The patient thought that this treatment made him less nervous, but it was noted that his intake was gradually increasing.

The patient was now put on 8 minims of adrenalin, t.i.d., by mouth. This failed to control the gradual rise in the intake.

Giving the adrenalin by means of a duodenal tube gave no better results.

The patient was next put on desiccated pituitary extract, posterior lobe (Armour & Co), in salol coated capsules. The dose was

started at one-half grain, t i d, and gradually increased to two grains, t i d, a c and at 10 P M The 10 P M dose was found to be necessary to control the nocturia

On the latter treatment the intake came down to between two and a half and three liters and remained there during the two weeks that the treatment was continued The patient stated that he felt better than he had since the onset of his trouble His headaches disappeared, he became less nervous He had no nocturia The number of stools decreased from 4 or 5 watery stools per day to one or two formed stools per day The patient stated that he was quite satisfied with two and a half to three liters of fluid per day His only complaint was some difficulty in getting to sleep at night This was relieved by giving eight minims of paraldehyde at bedtime

Before and during the treatment quantitative tests were made on the urine as follows for urea, uric acid, creatinine and chlorides Tests were also run on the blood for non-protein nitrogen, urea, uric acid, and creatinine These constituents were found to be practically normal in amount There was practically no variation in them after the urine became more concentrated

During the treatment with pituitary extract the specific gravity of the urine went as high as 1024 on the night specimen and 1019 for the day specimen

We next tried the effect of intra-muscular injections of pituitary liquid Single daily injections of 1 c c would reduce the output for about twelve hours, but during the next twelve hours there was a marked polyuria so that the total twenty-four hour output was not decreased Two injections of 1 c c each were effective in keeping down the daily output, provided the second injection was given at about ten o'clock at night Even with two daily injections the intake and output were not reduced below two and one-half liters This is no greater reduction than was obtained with the dry extract given in salol coated capsules by mouth

Whenever the patient was taken off all treatment his fluid intake and output increased in two or three days to seven liters or more

We now tried giving the pituitary extract powder to see whether it would be as effective as when given in salol coated capsules The powdered extract was given in a small amount of milk in two grain doses, t i d, a c and at 10 P M This method of treatment proved to be quite ineffective in controlling the polydipsia and polyuria Giving the powdered extract per rectum in four grain doses twice per day gave no results The patient was discharged from the hospital on June 15, 1921 At this time he was still keeping his intake and output under three liters

Since leaving the hospital the patient has been unable to secure a sufficient amount of the desiccated extract and he has passed as much as twenty liters of urine per day

He also complains of marked fatigue on slight exertion and since leaving the hospital he has been unable to do more than four hours work per day. The fatigue is followed by uncontrollable thirst. The patient feels sure, however, that if he could avoid exertion and could have the pituitary extract regularly, he could control his thirst at any time.

DISCUSSION

It is possible, in this case, that the marked hypermotility of the alimentary tract may so increase water absorption as to cause the excessive thirst, and incidentally the excessive urinary output. It is also possible that the pituitary extract may decrease the absorption of water either by limiting the intestinal motility or by increasing a local vaso-constriction.

The results obtained in this case would suggest that, in some instances at least, diabetes insipidus may be successfully treated by giving the desiccated posterior lobe substance of the pituitary gland by mouth, provided that it is given in such a way as to pass through the stomach unchanged.

Giving the extract in salol coated capsules seems to give a satisfactory solution to this problem.

SUMMARY

The possibility of finding a satisfactory method of administering post-pituitary extract by mouth was investigated. Reduced expense and increased convenience for the patient were the principle factors considered. The history, physical and laboratory findings in a case of diabetes insipidus are given. The progress of the patient under various types of treatment is recorded. It was found that by giving desiccated posterior lobe substance in salol-coated capsules the polydipsia and polyuria were as effectively controlled as with hypodermic injections of pituitary extract.

CHILDHOOD MYXEDEMA OR SO-CALLED SPORADIC CRETINISM IN NORTH AMERICA *

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The object of this paper is to present a study of cretinism in the United States and Canada as to its prevalence, pathology, symptomatology and treatment. The first case was reported by Jacobi in 1879. The first attempt to collect all the available data on the subject was made by William Osler in 1893, covering but eleven cases in all. This was followed by a more extensive investigation in 1897 in which he presented sixty cases. In the following year McPhedran reported seventeen cases which had occurred in Ontario alone. In 1901 John McCrae added twenty-three more cases found in Canada. These writers were of the opinion, however, that the number of cases in existence was far in excess of those reported. Murdoch in 1900, as the result of a questionnaire sent to institutions for feeble-minded throughout the country, was able to obtain information on sixteen cases, two of which, however, had already been reported by Osler. Howard, in 1907, made a statistical study of myxedema in America and collected one hundred cases, but did not deal with cretinism or cases under puberty. The next investigation was by Anders in 1918 on myxedema and cretinism, covering the period from 1905 to 1918 under the misapprehension that Howard had covered all the cases of cretinism from 1897 to 1905. Anders found 28 cases in the literature and added 43 unpublished cases obtained from institutions and other sources, but he failed to include 16 cases reported by Sill in 1905 and 41 cases by Heriman in 1914. M B Gordon supplemented the literature by 21 cases in 1918. Prior to the publication of Anders' article in 1920, the writer undertook this study at the request of the editor of *ENDOCRINOLOGY* and found additional

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case reports in the literature, which, with 5 personal unpublished cases, total 340 cases of so-called cretinism, these include the 60 of Osler. The prevalence of this disease is probably much greater than is indicated by the figures here given, as there are numerous references in the literature to cases which existed but had not been reported.

The data in this study will be primarily confined to the 280 cases reported subsequent to those by Osler.

GEOGRAPHICAL DISTRIBUTION

The locations of the 280 cases included 27 states and Canada, when the residence of the patient was not given, it was assumed to be that of the doctor reporting it.

Canada	52	Oregon	3
New York	120	Rhode Island	3
Pennsylvania	25	Maine	2
Indiana	12	Missouri	2
Ohio	10	Nebraska	2
Massachusetts	6	Arkansas	1
Minnesota	6	North Dakota	1
Virginia	6	Montana	1
Kentucky	5	Washington	1
Iowa	5	Kansas	1
California	4	Colorado	1
Maryland	3	Louisiana	1
Illinois	3	District of Columbia	1
Wisconsin	3		

It is readily seen from these figures that geographical location has no bearing upon the prevalence of this disease. Even though goiter is endemic in Canada along the St. Lawrence, in the Allegheny Valley of Pennsylvania and along the Great Lakes, not a single case of endemic cretinism was found and the incidence of so-called sporadic cretinism was no greater than in other regions.

NATIONALITY

It was very difficult to obtain statistics as to the nationality of the parents, in an endeavor to determine a foreign predominance, if any, because of the incompleteness of the data on all cases outside of New York State. Almost 50 per cent were reported from New York and Pennsylvania, two states with large foreign population. In New York City alone the cases of Herrman, Sill and Gordon, 84 in all, were known to consist of a predominating foreign element, Austrian, Russian and Italian. It is more than probable that the large foreign population in these two states accounts for the enormous excess over the other regions.

Munson studied the incidence of goiter and cretinism among the Indians of the United States and found that while goiter was of frequent occurrence among them, cretinism was rare. He states that 7 cases have been reported in which the mind was affected to a greater or less degree in persons with goiter and quotes Martin, who found a case of cretinism with a goiter in a girl of 12 years of age among the Indians of the Blackfoot Agency. He also states that Howard reported a case of an idiotic girl of about 19 years of age who had a goiter and whose mother was also goitrous.

CLASSIFICATION

Preparatory to undertaking such an investigation as this, it is necessary to have a working knowledge of some fundamentals of the underlying pathological processes existing in cretinism. Primarily, it was established by the committee of the Clinical Society of London in 1888 that in the conditions known as myxedema, sporadic cretinism, endemic cretinism, operative myxedema of animals and operative cretinism there is a pathological condition common to all, namely, the occurrence of morbid processes in the thyroid gland.

Since then very sharp controversies have raged as to the proper classification and terminology of the different forms of myxedema. Murray defines cretinism as "a condition which is due to diminished functional activity of the thyroid gland commencing before birth or in early life before 15." Osler amplifies this by calling it a "chronic condition characterized by disturbances of the growth of the skeleton and soft parts, a remarkable retardation of development, an extraordinary disproportion between the different parts of the body, and a retention of the infantile state with a corresponding lack of mental progress."

Myxedema, so designated by Ord because of the collection of what was assumed to be mucin in the subcutaneous tissues, has been studied from every conceivable angle and viewpoint by numerous observers and as a result the classifications of the disturbances due to loss of, or diminution in, thyroid secretion have been many. It is, therefore, with trepidation that the present investigator offers a new classification based upon the present study of the condition as found in America. He feels that the condition in this country is not the condition which is recognized as cretinism in Europe, that the term "sporadic cretinism" should be dispensed with, in so far as it applies to the disease in America, that cretinism should be limited to the type occurring in Europe and Asia and that the disease which is met with in this country should be considered as a separate entity, a pathological condition resulting from diminution or absence of thyroid secretion. Based upon pathological and etiological grounds, it can well be termed "childhood myxedema." The cases published in this country were reported under various terms such as congenital cretinism, congenital myxedema, myxedema in children, infantile myxedema, sporadic

cretinism, cretinism, etc In this study, no specific attention was paid to the term used by the original observer

The following classification is proposed

Myxedema—Types

- 1 Cretinism (Endemic)
- 2 Childhood myxedema (formerly called sporadic cretinism)
 - a Congenital myxedema
 - b Infantile myxedema
 - c Juvenile myxedema
- 3 Adult myxedema
- 4 Post-operative myxedema

Congenital myxedema (also known as congenital cretinism, thyro-aplasie, angeborene myoxidiotie, myxedematous idiocy, athyreosis congenita, myxedema athyreosum) has as its fundamental basis the complete absence of the thyroid gland Pineles insists that this term shall be limited to those cases in which there has never been the slightest vestige of a thyroid gland, and that it should be considered as an anomaly of embryological development According to this investigator, the presence of a goiter at birth, even though this goiter be composed of nothing but inert connective tissue and, the thyroid thus functionless, would be enough to prevent the case from being termed congenital myxedema The general consensus of opinion accepts this dictum, Horsley, however, claiming that this type is rare and that the children as a rule die at birth Their appearance is typical and the characteristic bone and cartilage changes with resulting deformities are already quite far advanced at birth

Infantile myxedema includes those cases in which the pathological disturbances in the thyroid originated before birth, but enough thyroid tissue persists to enable the child to live The symptoms are not present at birth, but develop within the first two to five years The thyroid gland may be either atrophied or enlarged

Juvenile myxedema is the term given by Parker to those cases which develop symptoms of myxedema as the result of some acute infectious disease or nutritional disturbance at any time during childhood These children are born with a normal thyroid, are normal at birth and in their subsequent mental and physical development, but following an acute disease show symptoms due to a progressive atrophy of the thyroid gland

Infantile and juvenile myxedema differ from congenital myxedema in that they are due to pathological processes in an already existing thyroid gland, whereas in the latter the gland has never been present

McCarrison describes another type of cretinism which he terms nervous cretinism, characterized by idiocy associated with cerebral diplegia and tetany due to congenital fibrosis of the thyroid and parathyroid glands No cases of this type have been encountered in American literature

Endemic cretinism is characterized by similar clinical manifestations as sporadic, but occurs only in countries where goiter is endemic. It will be dealt with more fully later on in the paper. There has not been a single case of endemic cretinism reported in the United States or Canada, and Osler considers that it is not at all probable from what he can learn that it has ever existed here.

ETIOLOGY

A question that has not as yet been settled is whether or not cretinism is a congenital disease. McCarrison claims that cretinism is always congenital, whether endemic or sporadic, except in those cases that arise postnatally from nutritional or infectional conditions. Kocher feels that "where the children are not born cretins, the thyroid gland in the majority of cretins has been congenitally so influenced that as the child grows, the sleeping abnormality in the gland begins to develop and the process continues until cretinism has been established. As can be seen, this is not strictly congenital, that is, the condition does not appear at birth and yet it is congenital because during fetal life through the blood or nourishment or drinking water or the mother, who herself may not have been a cretin and may have possessed a normal gland, the injurious tendencies were implanted in the thyroid gland of the fetus."

G. E. Smith, as a result of extensive study of fetal and maternal athyreosis among animals in goiter districts, claims that when an individual affected with thyroid disturbance becomes pregnant, unless that disturbance is counterbalanced by exceptionally favorable conditions, there will be a very seriously arrested development of the fetus, resulting in a more or less severe form of fetal athyreosis and grave disturbances will be produced in the maternal organism also. In our series in which goiter in the parents was mentioned, 13 gave a history of a goitrous mother at the time of the birth of the myxedematous child, while in 2 others, the mother developed a goiter subsequent to the birth of the affected child. In one family in which there were 12 children, the mother developed goiter after the birth of the second child, bore normal children until the birth of the patient, who was the eleventh, and then had a normal child in the twelfth pregnancy. In this instance the thyroid condition in the mother could not have been of very much etiological importance. There was no history of goiter in the father. Hodgins of Canada called Smith's attention to cases in which the father had tetany and the children had developed myxedema. McCarrison also cites the prevalence of endemic tetany in India as a disease of child-bearing women and corresponding to the locality of endemic goiter.

There are probably many cases of so-called sporadic cretins who become impregnated, but the only case on record in the literature is that reported by Townsend in 1897 and mentioned by Osler in his series. This woman was 38 years old, a typical idiot with the characteristic appearance of a cretin. A Caesarian section was performed

and a male infant was delivered. This child, while very feeble, did not show any signs of myxedema. He died in four hours. No autopsy was performed. Of course, the absence of signs of myxedema at birth would preclude the diagnosis of congenital cretinism, to use Pineles' term, still we cannot state definitely whether or not that child would have developed the disease later.

Heredity is probably a factor in the development of thyroid derangement, but it is difficult to estimate the extent of its influence. We can, however, safely state that the occurrence of but 13 cases of goiter in the mother indicates that it is probably of slight significance as an etiological factor in the production of childhood myxedema.

Tuberculosis, neuropathy, alcoholism, insanity and other degenerative strains have not been considered of much etiological importance by such investigators as Pineles, Tredgold and Murray, while Crotti and others feel that they have some bearing. Their incidence in the parents and family was small in the cases reported in America. On the mother's side there was a history of alcoholism, 2, tuberculosis, 8, insanity, 1, epilepsy, 3. On the father's side, alcoholism, 4, tuberculosis, 4, neuropathy, 1, paralysis, 1. Epilepsy, mental deficiency and goiter were found in both cousins and maternal aunts in several instances, but not of such frequency as to make them of etiological import. There were two instances of feeble-mindedness not of thyroid origin in brothers and sisters.

The presence of childhood myxedema in more than one member of a family was met with several times. Sanderson and Sill each reported one instance of 3 cases in one family, and Herrman two. Manson, Niles, A. Gordon, Koplik, McPhedran, Stewart, M. B. Gordon and Murdoch all cite instances of two in a family. In all, there were 4 instances of 3 in one family and 14 of two in a family. Manson's cases were twins, while Herrman reported a case in a twin with the other child normal. In a case reported by Busey there was a marked incidence of goiter and childhood myxedema in the family, the mother, maternal grandmother, a sister and two brothers of the mother had goiter. McCrae reported a case of childhood myxedema with a goiter in which both of the patient's sisters had goiter but not myxedema.

So-called sporadic cretinism does not seem to have any special predilection for either the first born or last born in the family, for in 100 cases in which the incidence of birth was noted, it was shown that in the majority myxedema occurred in children who were both preceded and followed by normal children.

Age at Time of Reporting, Where Given

Under 1 year	9	6 years	11	12 years	4
1 to 2 years	16	7 years	8	12 to 15 years	8
2 years	14	8 years	10	15 to 20 years	11
3 years	10	9 years	10	20 to 30 years	19
4 years	9	10 years	3	30 and over	13
5 years	13	11 years	3		

The sex of the cases where mentioned in this series, exclusive of Osler, shows the following male, 78, female, 152—a female preponderance of 2 to 1 in keeping with the findings of Osler in America

AGE OF INCIDENCE

The clinical manifestations of childhood myxedema depend primarily upon the amount of thyroid present and to a lesser extent upon the age of the child at the time of first appearance of the symptoms. Two, therefore, of the same physical age will present different stages of development if the disease appeared in one, say, at the age of 12 months and in the others at 8 years. Of 113 cases in which the date of first appearance of symptoms was noted the following distribution was found

At or from birth	13	From 18 months to 24 months	25
From 6 weeks to 6 months	10	From 2 years to 10 years	16
From 6 months to 12 months	40	Over 10 years	2
From 12 months to 18 months	7		

There were 13 cases in which the symptoms were noted either at birth or the child appeared abnormal practically from birth. The incompleteness in the majority of cases of detailed symptomatology and the meagerness of description prevents us from considering all of these 13 cases as those of congenital myxedema. The presence of a goiter in one case automatically removes it from the congenital type to that of infantile myxedema, if we adhere to Pineles' classification. In three cases in our series, however, those of Sill, Herrman and Koplik, there seems to be no question that the condition at birth fulfilled the requirements of congenital myxedema. Osler includes one in his series, the case of Friend.

Herrman's case was that of a male whose parents were cousins. The delivery was normal. The symptoms were recognized at birth, but first observed by Herrman at 7 weeks of age. The length of the child was 50 cm, the trunk was large, the forehead low, hair dry and scanty, eyes small and placed far apart, the lips thick, nose broad and flat, cheeks soft and flabby, tongue large and thick, the neck short and thickened, thyroid not felt. The chest was well formed, the skin characteristic, the face of a stupid appearance. The temperature was 96° F.

Koplik's case was that of a female child who directly followed in birth a sister who was also myxedematous. As the first child was still under the doctor's care, he had an opportunity to observe the symptoms from birth. The delivery was normal. The child became jaundiced at four days of age and continued so for several weeks. She was short and thick set, the extremities short, but not deformed. The skin was cool to the touch but not myxedematous, the tongue large, lips puffed, neck short and thick, the head oxycephalic. The thyroid was not felt. The child had a stupid look, did not cry until teased, was apathetic and dull, even the clapping of hands failing to

attract her attention. The doctor made his diagnosis on reduced temperature, marked stupidity, peculiar conformity of the extremities as compared with the trunk, hypertrophied tongue, wrinkled skin, thick lips, coarse cry, and the improvement on thyroid medication as evidenced by the child's becoming brighter, noticing its surroundings, cooing, smiling, and by the thinning of the tongue and the normal appearance of the face. The hemoglobin at the beginning was higher than later, even though the child was placed on thyroid immediately. Koplik felt that this indicated that the anemia develops as the disease progresses, but is not present in the early stages.

The subject reported by Sill was small at birth, with short extremities, which were cold to the touch. The skin was yellow and wrinkled like an old man's and hung loosely upon the body. The nose was flat and stubbed, the eyes far apart, lips thick, tongue large. There was a fatty tumor in the supraclavicular space. The child never smiled and was very apathetic.

SYMPTOMATOLOGY

The symptomatology of a fully developed case of childhood myxedema or so-called sporadic cretinism, as evidenced by the increasing number of case reports in the literature, is well known. Once observed, the general appearance and facies will always be remembered.

Head—There is a lack of synthesis forcing the sutures and the fontanelles to remain open for a longer time than normal with a resulting larger head, and yet there is the same physiognomy as in endemic cretinism. In the latter type there is a premature synthesis of the skull with a production of a broad nose, prominent lower jaws, low forehead, prominent cheek bones and large alae nasi. Due to the early synchondrosis between the os basillare and the sphenoid bone, the basal ganglia of the brain cannot develop. The fontanelles close earlier in endemic cretinism. In keeping with the general observation, we found a late closure of the anterior fontanel in nearly every case, the latest age at closing being 10 years. In another instance, both fontanelles were still open at 5 years.

Face—There is a stupid, dull look. The shape is round, moon-shaped, with a low forehead and wrinkled skin. The nose is saddle shaped, wide at the base but short and retrousse, the alae nasi are dilated. The ears are thick and everted. The eyes are placed far apart with narrow slit-like apertures, the malar regions are prominent, cheeks flabby and hanging, the lips are thick and everted, the mouth is wide open and drooling with a protrusion of the tongue which is enlarged, but without muscular hypertrophy. The face may show eczema.

Teeth—Delay in the time of eruption of both the temporary and permanent teeth is almost general. It sometimes takes years before the first set has fully erupted and an additional longer time before the appearance of the second set. In one case the permanent teeth

did not erupt until the age of 17 and only 3 had appeared by 21 In another subject 30 years of age a few of the deciduous set were still present The teeth in childhood myxedema are carious, brittle, short, irregular in their distribution and decay very easily

Neck—The neck is short with lipomatous masses in the supra-clavicular space

Thorax—Flatness of the thorax is characteristic

Abdomen—Potbelly and umbilical hernia are seen

Extremities—The arms, legs, hands and feet are very stocky, the fingers swollen, feet short and deformed, being too broad for their length, the toes are also swollen, producing an unsteady gait The general appearance is that of a dwarf The extremities are cold and blue at times Muscular co-ordination is delayed The most advanced age at which there was reported inability to sit was 3, inability to stand, 5, and backwardness in walking, 14 The gait as a rule is clumsy and unsteady

Skin—The skin is sallow, semi-translucent as in phlegmasia albolens There is edema and swelling of the subcutaneous connective tissue which is more marked in the face, tongue, lips and cheeks This seems more pronounced in the child than in the adult and because of the softer tissues imparts a much more myxedematous appearance

Genitals—There is lack of development of the genitals marked in both sexes with a delay in puberty There may also be undescended testicles in the male The oldest cases in which there were signs of delayed puberty was in a man of 30 who did not show any signs of a beard and in a woman of 20 who had not as yet menstruated Precocious development in both the primary and secondary sex elements were noted in a few cases in both sexes

Skeleton—The skeleton is smaller than normal, due to the persistence of the epiphyseal cartilage and retardation in the ossification along the epiphyseal line The delay in ossification is seen in the skull, and pelvis as well as limbs The spine generally shows lordosis, but at times kyphosis

Mentality—This ranged from a mental deficiency in the congenital myxedematous type to a slight mental aberration in the other forms In the congenital type, the children were dull, stupid, apathetic, leading a vegetative life of eating, breathing and sleeping They could not attend to their wants, they would sit still with neither a smile nor a cry Others showed no signs of defective mentality in the first months, but with time it was noticed that they neither cried or if so, very little, and paid no attention to other children In the older children of the infantile and juvenile types, backwardness in school was a prominent feature Delinquency in talking kept apace with mental deficiency Some did not talk at all or else gave expression to their meager thoughts in monosyllables, but never advanced to the

phrase stage The majority of advanced cases presented a guttural, harsh voice, giving vent to incoherent speech with a limited vocabulary

Koplik and Lichtenstein described a prominence of the antithenar eminence over the situation of the os pisiformis which they consider a part of the symptomatology of so-called cretinism They found it in all cases of this disease under their observation and also in other conditions like microcephalic idiocy and other degenerative states The only mention of this sign in the literature is that of Engelmann, who mentions it as one of the symptoms of cretinism, but does not state whether or not it appears in her case This prominence is immediately adjacent to the groove which separates the palm of the hand from the forearm It is distinctly localized to this portion of the antithenar eminence and viewed from the side rises abruptly from the above groove, giving a bayonet-like appearance It probably represents over-development of the small muscles of the inner border of the hand attached to the os pisiformis, as well as, perhaps, an enlarged condition of this bone itself A similar condition is seen on the foot of the domestic cat It might be caused by the act of crawling on the floor and supporting the weight on the inner border of the hands, but it was also observed in a myxedematous child only three months of age The authors cited consider it a congenital anomaly in degenerative children and have not seen it perfectly developed in a normal child

The onset of symptoms is early At birth, the child appears normal, but with time it is noted that it does not act normally, does not take well to the breast, seldom cries, is more or less dull and apathetic, is backward in teething and perhaps in crawling and in the majority of instances in talking When the child reaches a certain age, depending upon the amount of thyroid functioning, he stops growing or else slows down for a year or two and then ceases to develop From then on, his mentality and physical development cease to progress and he either remains at that mental age or else advances very slowly In some instances he may even retrogress and lose all the knowledge he had formerly acquired

In another form of childhood myxedema, the so-called juvenile myxedema, the child is born normal and functions normally until he is attacked by some acute infectious disease or some other acute pathological condition which produces acute thyroiditis and subsequent atrophy of the thyroid gland It seems in these cases that during this acute attack there is a call for thyroid on the part of the body which is supplied but at the expense of a diminished reserve There were 31 instances in this series in which the onset of the symptoms could be traced to a definite time following a definite acute attack Of this number 1 followed diphtheria, 3, scarlet fever, 6, whooping cough, 1, "fever", 3, pneumonia, 3, gastroenteritis, 4, jaundice, 1, vaccination, 1, acute thyroiditis, 2, cholera infantum, 1, sunstroke, and 4, weaning

The manner of onset of the symptoms differs. One child at 2 years of age could talk, stand and crawl, but following an attack of whooping cough, it became dull, inactive, and constipated, the skin became dry and harsh, the hair, which was curly, became straight and dry, and the child quickly assumed the typical myxedematous appearance. Sometimes there is first a change in disposition, followed by gradual assumption of the other symptoms. In some instances, the changes are more gradual as in one case following diphtheria at 11 months of age. The change was not noted until six months later, when the first symptom to make its appearance was decaying of the teeth and a sudden swelling of the face and body. In another case, there was a history of a so-called "cold on the lungs" at 8 months, followed by very slow development until the age of 3, when there was a permanent cessation of growth. Koplik reported 3 cases following several weeks' attacks of icterus neonatorum. The patients developed signs of myxedema at 6, 12, and 15 months, respectively.

Shields describes a case in a girl who was normal until the age of 10 months, when she had an attack of acute thyroiditis accompanied by fever, swelling of the thyroid and pressure of the trachea, but with no signs in the throat. The symptoms subsided in a week. Immediately growth and development ceased. At the age of 7 she was a typical cretin of low mentality.

Four of the cases showed signs of myxedema upon being weaned. The face broadened, nose flattened, and the subcutaneous fat increased in amount. In another case, dentition ceased and the few teeth the child had already had begun to decay. She never developed any new teeth. This would apparently indicate that mother's milk contains thyroid substance. A study of our series, however, does not bear this out. Of 20 cases designating breast feeding, it was found that 8 were at the breast at the time of the appearance of symptoms, 4 showed signs at weaning and 8 gave a history of breast feeding for periods ranging from 9 months to two and a half years with no immediate symptoms following weaning. Both Gordon and Herrman found that breast feeding had apparently no influence on infantile myxedema, for a number of their cases developed the condition while at the breast. In their large series neither reported any cases of immediate onset after the discontinuance of breast feeding.

An unusual mode of onset is described by Manson in male twins, 23 years old at the time of reporting. They were both wet nursed until 16 months of age and were apparently normal until symptoms set in. At the age of 11 years, one of them was suddenly seized with an inability to walk, was put to bed, recovered and then had a second attack six months later, which was followed by ataxia and epilepsy. The second brother did not show anything abnormal until 14 years of age, when he also developed ataxia. Both ceased growing at the time of their respective attacks and at the time of reporting, their mentality was that of half their age, corresponding to the time at

which they stopped growing physically The thyroid was non-palpable in both

A Gordon describes two cases of what is evidently juvenile myxedema complicated with diabetes mellitus The children were brothers, aged 3 and 4½ years, respectively Both complained of thirst, ravenous appetite and abundant, frequent urination with a gradual increase in mental dullness, apathy with outbreaks of excitement in the older, puffiness of the eyelids, edematous dry skin, dry hair, and in the younger the teeth were normal, but carious in the older The thyroid seemed to be absent in both The mother was obese and diabetic, while the father was neuropathic While myxedema in adults attended with glycosuria is not rare, myxedema with true diabetes mellitus is

The total energy requirements in cretins is 18 to 25 per cent below normal as shown independently by Du Bois and Talbot With this decreased metabolism, it is to be expected that the mortality of these children would be high and their resistance low Packard and Hand quote several instances of the lowered resisting power of myxedematous children Still there were 13 subjects in this series over 30 years of age, one of them reaching the age of 64 after having shown symptoms when two years old

PATHOLOGY

According to Rushton Parkei, there are three groups of cases (a) with absence of the gland, (b) with atrophy of the gland, (c) with enlargement of the gland A diagnosis of complete absence of the thyroid cannot be made with certainty during life The slightest strand of connective tissue may reveal its presence by means of the microscope Excluding Osler's cases, there were 112 in which mention was made of the condition of the gland The terms, "absent," "not palpable" and "not felt," were used interchangeably It was noted either absent or not felt in 100 cases, atrophied in 2 and hypertrophied in 10 Complete absence is found only in congenital myxedema Such a case was reported by Friend in Osler's series In apparent absence of the thyroid careful microscopic examination of sections made through the usual site of the gland or neighboring structures may reveal rudimentary alveoli or anomalies as in MacCullum and Fabian's case in a 13 year old girl There were no signs of either the superior or inferior thyroid artery Two large parathyroid bodies lay on each side just at the lower limit of the larynx Below and outside of the parathyroid, on each side were found small lobulated cystic structures At one side of the cyst in each mass was a little glandular tissue formed into acini which had scarcely any lumen It seems unquestionable that this was thyroid tissue, although it did not resemble the normal very closely Dense fibrous tissue, in which there were occasionally very small alveoli, was found, probably representing scanty remains of the thyroid lobes No trace of the thyroid could be found in small sections of tissues in front of the

larynx or hyoid bone. Sections through the root of the tongue showed thyroid tissue much better preserved than that in the neck, showing numerous alveoli containing colloid. The epithelial cells were cubical, some increased in size by the enlargement of the nuclei which took on a deep stain showing a functioning gland with compensatory hypertrophy. The parathyroids were normal.

Atrophy of the gland is generally found in that sub-group described as juvenile myxedema. Parker collected 10 such cases in England. Atrophy during childhood generally follows an acute infectious disease or disturbance. Osler gives a very excellent description of the gland in this type. Packard and Hand reported some unusual findings in a case of infantile myxedema. The child was breast fed until 20 months of age. When 4 months old she had an attack of apparent loss of consciousness. At the time of death she was 6 years of age and prior to that time could not walk or talk, was apathetic and fat. Thyroid had been administered with a rapid improvement in the symptoms, but she eventually died of typhoid fever after having been sick for 5 weeks. On autopsy the alveoli in the thyroid were found to be marked off by bands of white fibrous tissue, especially about the blood vessels. The cells varied in size, acini were small, many containing no colloid whatever, the total of the colloid material being smaller in amount than the normal. There were calcareous changes in the walls of the blood vessels, the media and at times the intima and adventitia showing a formation of cavities surrounded by calcareous deposits. There was found no other mention of this change in the literature. The hypophysis and thymus were both enlarged.

There were 10 cases in this series which presented a goiter. Of Osler's 60 cases goiter was present in 7, making a total of 17 goiters in 340 cases, an incidence of 5 per cent as compared with the 44 to 60 per cent found in true endemic cretinism. In one of the cases the thyroid enlargement was noted a few days after birth, from which time it became progressively larger. In another case there was a cyst about 2 inches in diameter in the right lobe of the thyroid, with a fibrosis of the left lobe.

The blood examinations reported show anemia with a hemoglobin range from 18 to 75 per cent. There was a decrease in red blood cells, in some cases a decrease in white blood cells, at other times an increase. The differential count was practically normal.

DIAGNOSIS

The diagnosis of childhood myxedema is comparatively simple. It must not be confused with minor types of hypothyroidism on the one hand or endemic cretinism and mongolian idiocy on the other.

Differential Diagnosis

<i>Mongolian Idiocy</i>	<i>Childhood myxedema or So-Called Sporadic Cretinism</i>
Oblique palpebral fissure and superciliary margin	Lids swollen, almost closing eyes
Tongue is hacked, furrowed, beef steak appearance	Tongue large and protruding, but not furrowed and hacked
Lips normal in size	Lips large and prominent
Complexion waxy and pale	Complexion muddy yellow
Skin not infiltrated	Skin infiltrated and wrinkled
Fingers thick but tapering at the points with incurving of the little finger	Fingers have blunt points
Abdomen not protruding	Abdomen protruding
No pads of fat in supraclavicular region	Pads of fat present in supraclavicular region
Thyroid gland can be felt	Thyroid cannot be felt, as a rule
Mobile	Less mobile, apathetic

Differences between Childhood Myxedema and Endemic Cretinism

1 Location Endemic cretinism, according to the majority of the students of this subject, can occur only in regions where endemic goiter prevails. Sporadic cretinism, so-called, can occur anywhere, even in endemic goitrous districts. Even though endemic goiter is prevalent in Canada along the St. Lawrence and in America along the Great Lakes, in the Alleghany Valley of Pennsylvania, in Ohio, parts of New York, Ohio and Minnesota, not a single case which can be accepted as endemic cretinism has been reported in any of these regions nor is the incidence of childhood myxedema any greater in these places.

2 Etiology The role of the thyroid in endemic cretinism is not uniformly interpreted by all investigators. Kochei and Wagner claim that clinical manifestations of endemic cretinism are due to thyroid disturbances alone. Kutchera, Bircher and Ewald, on the other hand, think that it is due to some other factors in addition to thyroid dyscrasia, feeling that it is a physical as well as an intellectual degeneration not solely dependent upon thyroid pathology, but to some other additional damaging influences in other organs of the body as a consequence of the endemic. One of these causes is that the endemic has been exerting its influence upon the organisms of these individuals throughout successive generations, the degree of the toxicity depending upon the amount of noxious material present in the organism and also in the locality. This latter view is strengthened by the birth of endemic cretins only in endemic locations, for a goitrous mother will bear a well-developed, normal, intelligent child if she removes from the endemic territory.

The role of the thyroid in childhood myxedema or so-called sporadic cretinism has been accepted and proved.

Influence of goiter in the mother In almost every case of endemic cretinism, there is a history of goiter in one of the parents

In childhood myxedema, in America, there was an incidence of 13 cases of goiter in the mother and of none in the father out of a total of 340 cases, an almost negligible influence

Psychic factors Fright, worry, mental depression and "antenatal impressions" are reported as prominent etiological factors in the production of endemic cretinism, but are of absolutely no importance in childhood myxedema

Illness in mother during pregnancy such as rheumatism, tetany, malaria and nutritional factors in both the mother and the child, both antenatal and postnatal, were of no etiological importance in the production of childhood myxedema in our series, but are admitted to be causative factors in the production of endemic cretinism by McCarrison and others

3 Differences in the body skeleton In endemic cretinism, the retardation of ossification is much more irregular than in childhood myxedema, certain epiphyses and synostoses undergo normal ossification, while others do not There is a premature synostosis between the os basillare and the sphenoid with a consequent earlier closing of the fontanels In the myxedema of children, the enchondrial and periosteal ossification is considerably retarded and takes place later in life The fontanels remain open for a long time

4 Duration of disease In endemic cretinism, the disease remains stationary and as a result, the subjects live to an old age Ewald makes the statement that he has never seen nor heard of a victim of sporadic cretinism living beyond the 30th year This is based upon observations in Europe Crotti takes the same view That what has been called sporadic cretinism in America is probably not the same disease as that so styled in Europe may perhaps account for the finding of 13 subjects in our series who were beyond the 30th year, one still living at the age of 64 at the time of publication Osler noted 7 past the age of 30 in his series

5 The presence of goiter The incidence of goiter in endemic cretinism has been rated at from 44 to 60 per cent by different observers Pineles classifies sporadic cretinism as a sub-variety of congenital myxedema and insists that the presence of a goiter immediately stamps a case of cretinism as of the endemic type By dispensing with the term "sporadic cretinism" for the cases observed in America, we can avoid the pitfalls of a complex terminology as to what is and what is not endemic cretinism In our series of childhood myxedema, there were 17 cases of goiter out of a total number of 340, an incidence of but 5 per cent

The thyroid gland in both endemic cretinism and childhood myxedema, when enlarged, may either be completely fibrosed or more commonly the gland is in a state of partial fibrosis and hyperplasia

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It may be the site of cystic enlargement or interstitial hypertrophy with a resultant non-functionating gland

TREATMENT

In the treatment of endemic cretinism, it has been demonstrated time and again that thyroid extract is not nearly as efficacious as in the so-called sporadic type. This means that the former disease lies further back than the loss of the thyroid, both the goiter and the cretinism resulting from the same influence or else the condition is a complex one and only partly of thyroid origin.

In the treatment of childhood myxedema there is great variance as to dosage, the form of gland used and the method of administration. The dosage ranged from 3/10 grain a day to 45 grains a day of thyroid extract. Some used the powder, others the extract in tablets. To make matters still more complicated, the dose was designated as so-and-so many tablets without indicating the content of the tablets.

There can be no uniformity in the treatment of this condition until the thyroid extract used is standardized in the process of manufacturing and in the designation of dosage. While all the products must conform to the requirements of Pharmacopeias, there is no law governing the standardization of the processes of drying, defatting, and refrigerating of the original gland substance. The different methods in vogue by the various packing houses and endocrine manufacturers and the consequent products differ in many respects.

At the present time, to insure beneficial results, it is best to decide upon a certain manufacturer's product and continue to prescribe it by name, because of the variations in strength of the supposedly same dose of different firms.

The dosage seems to depend upon individual susceptibility and not upon either weight or age. The amount of thyroid that can be taken without producing toxic symptoms depends upon the amount of auto-genous thyroid of the subject as well as his susceptibility to the hormone. There is no means known at present of ascertaining these, hence it is best to start with small doses and work up to the point of tolerance. The tolerance may vary from two grains of thyroid a day to more than 45 grains (Manson's case). Wood, in discussing Lamb's case, referred to a child who by mistake took 20 to 30 tablets of thyroid extract at one time without any harmful effects. He did not state the dose of each tablet. In contradistinction to this, Lamb's patient developed signs of acute thyroiditis when more than 1/2 grain a day was taken. When first introduced, large doses were in use, but now there seems to be a swinging toward the other extreme, for the present tendency is towards smaller doses at the onset with a gradual increase. The tolerance is thus increased, so that a child who was unable to take 1/2 grain at the onset can be given two or three grains within a short time. The method of some is to administer the gland on alternate weeks with intervening periods of rest, while others prescribe it

for a month and then rest. Still others advise a continual administration, with a graduatory upward dose.

The reaction produced by a dose beyond the child's tolerance is essentially that of acute thyroiditis and comprises nervous, gastrointestinal and cardio-vascular symptoms such as extreme restlessness, crying spells, loss of sleep, vertigo, headache, diarrhea, vomiting, syncope, tachycardia, flushed face, rapid rise in temperature, falling out of the hair and general exhaustion. Upon the appearance of any untoward symptoms, the thyroid must be immediately discontinued, to be resumed only when these have disappeared. Upon resumption, it is advisable to start with a smaller dose.

The results obtained in the treatment of childhood myxedema has fully justified the hopes held out by Horsley, Murray and Mackenzie years ago. It is the one triumph of organotherapy that is unquestioned. We will not attempt to essay a statistical analysis of the results obtained in this series. Many cases were absolutely cured, others were ameliorated, while still others were not influenced at all. The outcome depends upon several factors: the amount of thyroid deficiency, the time of the onset of the treatment, the age of the patient, and the regularity with which the treatment is carried out, together with the length of time under treatment. The secret of success is early diagnosis, with early and long continued treatment. The physical defects such as those of walking, teething, crawling and bodily development are more amenable to treatment than the mental defects. In children with pronounced mental retardation, the mentality may improve to a large extent, but still never reach the normal. Some always remain a few years behind others of their age, while others develop up to a certain mental age and then remain stationary.

The initial signs of a beneficial result are generally a rise in temperature and an improvement in the appetite. There may be a preliminary loss of weight followed by an increase, with an accompanying increase in height. The child becomes brighter, shows an interest in its surroundings and in itself. The hair and skin become softer in texture and the latter loses its myxedematous appearance. The shape of the face changes. Constipation and even enuresis are cured. Abdominal distention is reduced and sometimes umbilical hernia disappears. The blood may show an increase in the hemoglobin. Du Bois found that the total energy metabolism was raised almost to the normal on the third day of treatment.

SUMMARY AND CONCLUSIONS

1. Cretinism as it exists in Europe does not exist in America. Not a single case of true endemic cretinism has ever been reported in America. The sporadic cretinism as encountered in Europe differs from what has been termed the same disease here. There seems to be such an indefinite understanding as to just

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what is meant by the term sporadic cretinism, that it seems advisable to dispense with it, at least in America, and to restrict the term cretinism to the endemic type found in Europe and Asia. The so-called sporadic cretinism of America is really an intense and exaggerated form of hypothyroidism and as such should be known by the term of childhood myxedema or myxedema in children.

2 Childhood myxedema is not uncommon in America, although there are some localities where it is not often seen. The incidence is probably greater than that indicated by the 340 cases reported in the literature. There were only 4 of the congenital myxedematous type and 31 cases of the juvenile type. The rest were of the infantile myxedematous type.

3 The greatest number of cases was found in New York and Pennsylvania. This finding is probably due to the large immigrant population in those two states. Geographical location had no apparent bearing upon the prevalence of this disease.

4 Hereditary influences appear to be of little etiological importance, although there were several instances of more than one case of childhood myxedema in the same family.

5 The incidence in females was twice as great as in males.

6 Treatment with thyroid gland products is of great though not unfailing benefit. Some cases are curable. Mental retardation is not so amenable to treatment as physical deficiency. Prognosis depends upon the age at which treatment is instituted and upon the regularity and continuance of treatment.

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THE EFFECT OF BODY TISSUES OTHER THAN THE THYROID UPON THE BASAL METABOLIC RATE

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During the past 20 years the rôle of the body tissues in regulating the basal metabolic rate of the organism as a whole has been thoroughly studied. Errors in technic and lack of careful controls have rendered much of this work unsatisfactory, but reports of great value are to be found in the literature. The thyroid gland has been more carefully studied than any other tissue, as it seems to be the gland of internal secretion which exerts the greatest regulatory influence on the rate of oxidation in the organism. So much has been written on this subject, and the reports have been so thoroughly summarized in recent articles (1) that the rôle of this gland will not be considered here. It must be understood, however, that the effects produced by extirpation of the thyroid and feeding of its active principle are usually of far greater magnitude than those ascribed in this article to other organs. Aside from effects due to the nervous mechanism (2), there are changes in the basal metabolic rate which are caused by other tissues in the body. The object of this paper is to show the present status of our knowledge of this subject by summarizing valuable work reported in the literature. In this way possible fields for further investigations may be suggested.

As there are three general types of investigation the literature falls into three groups: first, extirpation of the various organs, second, feeding of dried organs, or of their active principle, and third, injection of active principles or organ extracts. All of these experimental procedures may distort the physiological activity of organs not under immediate consideration. This factor is perhaps of least importance in the feeding experiments where surgical manipulation is not involved. But since digestion may render the active principles inert, only positive results are of value in this type of investigation. By extirpation of organs, their regulatory influence on other tissues may be

observed, but such a procedure, of course, merely demonstrates the effect of elimination and allows no opportunity for the observation of hyperactivity. The poorest of the three methods seems to be the injection of usually very large quantities of active principles of the organs. This produces a picture which is pharmacological rather than physiological and may not really show the normal function of the organ. All three methods, therefore, have distinct limitations, but they may still give good evidence in regard to the general physiological influence of the tissues. The difficulty in studying cases of deranged internal secretion in man lies in the fact that in most cases there are pluriglandular disturbances and not sharply defined abnormalities of a single gland. Under these conditions it is quite impossible to determine the influence which each gland may be exerting.

The Pituitary Benedict and Homans (3) removed the anterior lobe of the pituitary gland in the dog, and noted that with the deposit of fat, which began about a month after the operation, there occurred a drop in the production of CO_2 per kilo of body weight. This work was very carefully done. Some stress must be laid upon the fact that the experiment extended through many months, for when operated on the dogs were not fully grown, and probably their metabolic rate per kilo was higher than when they were adult. It is also to be noted that according to Lusk (4) the mere retention of animals in cages for long periods of time causes a reduction of their metabolic rate, though this was controlled in one of their experiments. It is, therefore, questionable whether the drop of 10 to 35 per cent in the metabolic rate per kilo is entirely due to removal of most of the hypophysis. Other evidence, however, corroborates the observation that the pituitary plays some part in the regulation of metabolism.

Aschner and Porges (5) removed the whole anterior lobe of the pituitary of a six weeks' old dog. When 10 months old the animal was small and undeveloped, with a metabolism lower than that of normal animals. For this experiment there are, however, no very good controls.

Sack (6) and Schafer (7) in studying white rats found that feeding the anterior lobe and whole gland of the pituitary had no

effect on protein metabolism. They did not study the gaseous metabolism.

In human beings, however, changes in the pituitary gland are often associated with slight effects upon the metabolic rate. Magnus Levy (8) thought these cases always associated with disturbances of other glands. Boothby (9) has observed that apparent over-functioning of the anterior pituitary may cause a rise in the metabolic rate, while hypopituitarism may be associated with a rate somewhat below normal, although there is little evidence that the secretion of any part of the gland is concerned with the normal rate of cellular combustion. Means (10) has found a reduced metabolism in cases of obesity due to hypopituitarism. Bernstein (11) found two cases of acromegaly and one of hypophyseal dystrophy in which the total metabolism fell within normal limits.

After intramuscular injection of extracts of the pituitary, Bernstein and Falta (12) observed acute changes in the respiratory metabolism. Injection of a protein-free extract of that portion of the gland which is of nervous origin,—that is the usual pituitrin,—caused a rapid increase in oxygen consumption and an increase in CO_2 production which did not reach its maximum within three-quarters of an hour. Except for a slight rise immediately after injection the respiratory quotient did not change. There was, therefore, an increase in the metabolism after the injection, but no change in the relative percentages of the various foodstuffs burned. The blood pressure was not markedly affected. Sturgis, Wearn and Tompkins (13) tried similar experiments, using 1 cc of pituitrin. In eight subjects studied, seven showed no noteworthy effects in the metabolic rate, but one showed a rise of 13 per cent over the basal value. This is directly opposed to the observations of Bernstein and Falta.

Injection of the anterior lobe by Bernstein and Falta (12) showed quite a different picture. A protein-free acid extract of the glandular portion of the hypophysis was used. A short while after intramuscular injection of this extract both the CO_2 and the O_2 exchange fell markedly, the oxygen absorption decreasing the more rapidly so that at first the respiratory quotient rose sharply. This was only temporary, however, and as the

CO₂ elimination continued to fall the respiratory quotient soon reached its original level. This reduction of the basal metabolic rate lasted about an hour. On experiments such as these, however, too much stress can not be laid. The injection of such large doses of glandular extracts produces effects which probably do not represent clearly the function of the active principles during life, and which may not even be caused by the active principle. This type of work should be regarded as demonstrating the pharmacological rather than the physiological action of these tissues. These experiments have not been confirmed.

The studies of the pituitary, therefore, suggest the following conclusions

- 1 Removal of the anterior lobe causes a mild reduction in the basal metabolic rate which does not develop for weeks after the operation

- 2 Feeding experiments, which are not numerous, show no effect

- 3 Injection of the glands has a marked influence on the metabolic rate, but the effects so produced may not indicate the usual physiological action of the glandular secretions

- 4 While there is in man a tendency toward an increased metabolic rate with hyperpituitarism and toward a lowered rate with hypopituitarism, it is not clearly shown that these slight changes are caused primarily by the functional disturbances of the pituitary alone

The Gonads The literature on the relation of the gonads to the metabolic rate is neither very full nor very convincing. Most of the work has been done on animals before and after castration. While such studies strongly suggest that removal of the gonads causes a slow but definite reduction in the rate of metabolism, investigation of the effects of the internal secretions of the gonads in man has not clearly supported the results of animal experimentation.

Loewy and Richter (14) in their studies of the respiratory metabolism of a male and a female dog before and after castration found a decreased oxygen absorption after castration. This was more marked in the female than in the male, amounting, three weeks after operation, to a fall of 5 per cent in the metabolism per kilo of body weight. Three months after the opera-

tion a decrease of 18 per cent was found. When tablets of oophorin" were fed to the female the metabolism rose not only to the original normal rate, but to 50 per cent above normal. Pachtner (15) is reported to have confirmed these results, but Leo Zuntz (16), who later fed oophorin to the same dog which had been experimented upon by Loewy and Richter, could obtain no such increase in the metabolic rate as they reported.

Mullin and Bailey (17) in very careful work upon two female dogs found that the distinct fall in the basal metabolic rate following castration was of very slow onset. In one dog this decrease was 17.5 per cent per kilo per hour, and in the other it was 14.2 per cent. Working on white rats, Kojima (18) also obtained a diminished metabolic rate after castration. In four male rats he found the excretion of CO_2 per kilo of body weight to be 28 per cent lower than normal three weeks after operation. Seven weeks after gonadectomy this same low rate was still maintained. Similarly, Kallestinoff (19) has shown that the nitrogenous metabolism falls after castration, but as his work is very poorly controlled but little value should be ascribed to it.

In contrast to the results of these various authors, Luthje (20) reports no difference between the respiratory exchange of normal and castrated animals. This may be perhaps because he did not use the animals upon which he later operated as controls and because separate controls are not very satisfactory in a series of a few experiments.

That there is some interrelation of the thyroid and the sex glands in their effect upon the metabolic rate is suggested by the experiments of Rovinski (21), a pupil of Korentchewsky, who studied the effect of castration upon animals whose thyroid had previously been removed. In a long thesis published in 1913 he reports the results of experiments which indicate that although a fall in both nitrogenous and gaseous metabolism is usual after gonadectomy, it may not be constant. In the intact animal he finds this to be more marked than in thyroidectomized animals. From this Korentchewsky (22) concludes that the effects of the thyroid and the sex glands upon metabolism are synergistic, and that at least a large part of the changes following castration may be explained by the influence of the thyroid.

Leo Zuntz (23) in his experiments on the metabolism of castrated women determined the metabolic rate before and after removal of the ovaries. All the women were menstruating before the operation. In no case did he find a fall in the rate of metabolism within the first seven weeks after castration. Later there was a fall in some cases and not in others. After feeding his patients with large doses of oophorin the basal metabolism increased very slightly and thus confirmed the results he obtained by feeding oophorin to the dog upon which Loewy and Richter had worked.

In contrast to these results, Tierney (24) reports that in a patient whose pathological picture suggested pure ovarian insufficiency he found the basal metabolic rate to be 13 per cent below the average normal*. But he states that in his experience "primary gonadal insufficiencies, as a rule, have not shown such a decided decrease in the basal metabolic rate."

Snell, Ford and Rowntree (25) have published a preliminary statement in which they report a rise in the basal metabolic rate of women during menstruation,—a result which L. Zuntz (26) did not find in his two subjects. Recently Blunt and Dicke (27) have studied a large series of women and have not been able to demonstrate any definite change in the basal metabolism during menstruation. They have also found no rhythmical periodic variation.

All the literature seems, therefore, to indicate that the removal of the gonads causes in animals a rather slow fall of metabolism, which amounts to about 15 per cent three weeks after castration. The view held by Korentchewsky (22) suggests that this fall may be dependent upon the presence of the thyroid gland, and that it may be due solely to the interaction of the thyroid and the sex glands. Far too little work has been done to justify us in drawing clear-cut conclusions. More cases should be studied both before and after operation in order to confirm the fact that loss or absence of the gonads causes a slight reduction of the basal metabolic rate. There should also be further work on the effects of glandular feeding and of the marital state, before any definite conclusions are drawn as to the influence of the gonads upon metabolism.

*DuBois and DuBois also Aub and DuBois

The Spleen In a recent article Danoff (28), working under Asher's direction, reports the effect of removal of the spleen of white rats. Using Haldane's method to determine the respiratory metabolism, he found a rapid increase of about 50 per cent in the metabolic rate after splenectomy. This progressed until death, which, in the four animals successfully studied, occurred within ten days after the operation. It is claimed that white rats do not live longer than this after splenectomy. After the operation the animals perspired freely and the excretion of urine was markedly increased. To this work there are two objections: first, no indication of the temperature of the animals is given, and second, Danoff does not state whether the animals were active either before or after operation. In the same year that this article was published, Tomkins, Brittingham and Drinker (29) reported the results of a study of two cases of splenic involvement. One case of Banti's disease showed a metabolic rate 8 per cent above the normal of the DuBois linear formula. The other case, of splenic anemia, had a metabolic rate 5 per cent above normal before splenectomy. After removal of the spleen the metabolism of this subject was found to be 15 per cent below normal. These results are directly opposed to the findings of Danoff.

Korentsehewsky (30) also studied the effect of removing the spleen in three male dogs, and could find no marked effect upon either the nitrogenous or gaseous metabolism. King (31), who did not study the respiratory metabolism, found only a slight increase in the nitrogen excretion. There were no striking changes in carbohydrate or fat absorption, or in the calcium, chloride or endogenous uric acid excretion. Most of the evidence, therefore, indicates that the spleen does not markedly influence the metabolism.

The Blood The effect of abnormal conditions of the blood upon the metabolic rate has been studied by several investigators. In man, Kraus (32), Bohland (33), Magnus Levy (8) and Meyer and DuBois (34) have found a somewhat increased metabolic rate during anemia, but this increase is so slight as to fall almost if not quite within normal limits. Tomkins, Brittingham and Drinker (29) agree with these findings and state that the basal metabolic rate oscillates about the levels usually accepted as

normal It therefore seems fair to conclude that even severe anemia does not markedly affect the basal metabolic rate, but may raise it slightly

Leukemia, on the other hand, causes a very sharp increase in the metabolism as has been shown by Grafe (35), Magnus Levy (36), Kraus (32), Bohland (33), and Murphy, Means and Aub (37) This increase is about the same in both the lymphatic and myelogenous types and usually is as large as 40 to 60 per cent At least part of this rise has been ascribed by Grafe to the high metabolism of the young white blood cells

The Pancreas The results obtained by the various investigators after removal of the pancreas of animals are for the most part in agreement La Franca (38) successfully removed the pancreas of two dogs and found on the first day after operation that their respiratory metabolism had fallen The metabolic rate began to rise after this, and was maintained for several days at varying levels far above the original basal rate One of the dogs died of peritonitis No reports of autopsies are given and as no figures for the nitrogen excretion are reported the D N ratio cannot be calculated There is, therefore, no way of determining just how completely the pancreas was removed Verzar (39) also found that the rate of metabolism fell immediately after removal of the pancreas Six or seven hours after the operation he shows that this decreased about 8 per cent in curarized animals, but as the operation was accompanied by a disturbance of other organs and a marked fall of blood pressure this drop in metabolism cannot be considered significant In agreement with the results of La Franca, Mullin and Kramer (40), Falta, Grote and Staehelin (41) and also Moorehouse, Patterson and Stephenson (42) have found that the basal metabolism rises after pancreatectomy, the former authors reporting a rise as great as 42 per cent in the fasting rate This is, of course, associated with marked changes in the relative percentages of the foodstuffs burned in the body Carbohydrate is not utilized and the protein metabolism markedly increases This rise in metabolism may be ascribed to the specific dynamic action of the increased protein burned rather than to any stimulation by the absence of pancreatic tissue Therefore it is not fair to

draw the conclusion that the pancreas normally acts as a depressor of the metabolic rate

In man the effect of diabetes upon the basal metabolic rate has not been absolutely determined. The variations observed are probably due to the types of controls and to standards of metabolism used. In mild cases it is generally agreed that the metabolic rate is normal. In severe cases, two apparently antagonistic factors are found: first, a high protein metabolism which raises the rate because of the specific dynamic action of the protein, second, the undernutrition and emaciation which tend to lower the rate. Benedict and Joslin (43) think that in their severe cases of diabetes there was an increase of 15 per cent in the metabolic rate. Lusk (44) criticized this work, and thought that the results showed only an increase of about 5 per cent. Allen and DuBois (45) found no increase even in very severe cases, while Gephart, Aub, DuBois and Lusk (46) found in severe cases of diabetes that the metabolism was reduced after prolonged fasting. In one case in which the fasting protein destruction had reached such a very high level that 27.5 grams of nitrogen were excreted per day they found that the metabolism was 15 per cent and 7 per cent above the normal rate.

The Liver The liver plays so large a part in the metabolic activities of the organism that it is of interest to know its effects upon the general rate of metabolism. Grafe and Denecke (47) removed the liver after first making an Eck fistula. Their animals lived for four to fifteen hours after the operation. With a drop in body temperature of over 2°C , there occurred a decrease of as much as 33 per cent in the metabolism. Part of this may be accounted for by the fall of body temperature and possibly also by shock (48), although no blood pressures are recorded. The work of Mann (49) suggests, on the other hand, that this decreased metabolism may be due to an absence of glycogen and an inability normally to break down the amino acids, without the liver. According to this view, then, the liver would not be a regulator of metabolism but rather a storehouse, and the mechanism for accomplishing catabolism, and the reduced metabolism found by Grafe would be due, in part at least, to a lack of available foodstuffs. The metabolic rate of men with very severe liver disease has been shown by Aub and Means (50) to be essentially

normal, and they, therefore, conclude that in man at least the liver is not a regulator of the metabolic rate

The Thymus The effect of thymectomy in rabbits has recently been studied by Ruchti (51) in Asher's laboratory. He operated on four rabbits whose average age was ten weeks and obtained no evidence of clearly marked effects upon the respiratory metabolism. In his postmortem examinations he controlled his operations by microscopic inspection of sections of suspicious tissue.

The Parathyroids Several investigators have studied the effect of removal of the parathyroids upon the basal metabolic rate. Kojima (18) found that five parathyroidectomized male rats showed no change in the CO_2 excretion per kilo of body weight thirty days after the operation. Since there was no thorough search for accessory parathyroid tissue this work is somewhat open to question, even though postmortem examination showed no accessory parathyroid tissue present in the thyroids. He also found that parathyroid feeding had no effect on the rate of metabolism. An article published two years later by Loeffler (52) reports the study of a case of chronic tetany four years after a massive thyroid extirpation. The basal metabolism in this subject was found to be 18 per cent below the average normal figures of Aub and DuBois. Part of this decrease might, of course, have been due to the lack of thyroid tissue in the body. Careful autopsy one year after the determination of the metabolic rate disclosed no parathyroid tissue although parenchymatous thyroid was present. In contrast to Loeffler's results, Rovinski (21) has demonstrated an increased metabolism in two dogs whose parathyroids were badly injured or removed during thyroidectomy. His observations were made about a month after operation at a time when the animals showed little or no tetanic tremor, but in spite of this fact and the removal of the thyroid gland, there was an increase of about 20 per cent in the nitrogenous and gaseous metabolism. Pavlov in 1913 reported in the publications of the University of Craeow the results of a study of the gaseous exchange and the metabolism after removal of the parathyroid glands, but this work is at present inaccessible (53). There is, therefore, evidence that absence of the para-

thyroids may produce every possible effect and no definite facts have been really established

The Adrenals Bernstein and Falta (12) have found that when 1 mgm of adrenalin is administered subcutaneously the rapid rise of oxygen consumption which results reaches its maximum about an hour after the injection. The carbon dioxide excretion also markedly increases within the first five minutes, but then falls so gradually that it is still above normal at the end of an hour. Because of this difference in the two curves the respiratory quotient is above normal for the first twenty minutes after injection. More recent and much more complete studies have been made by Tomkins, Sturgis and Weain (54) and by Sandiford (55). They agree that intramuscular and subcutaneous injections of adrenin invariably cause an increased heat production in normal man, and that this is usually accompanied by a rise of the respiratory quotient which suggests an increased utilization of carbohydrates.

The metabolic effects of removal of the adrenal glands of animals were first observed by Gradinescu (56). He found that the basal metabolic rate dropped markedly, but part of this fall may have been due to the lower body temperature after the operation. Aub, Bright and Forman (57) studied the effect of removal of the adrenal glands of cats. They found that even when the blood pressure and temperature were kept normal after the operation the metabolic rate fell markedly about 24 hours after adrenal extirpation. It continued, until the terminal collapse, at a level about 25 per cent below the previous normal. Their animals lived more than five days after the operation. In anesthetized animals they made observations (hitherto unpublished) that the basal metabolism decreased promptly after adrenalectomy, but that this decrease could often be eliminated by the intravenous injection of adrenalin. Marine and Bauman (58) confirmed the decrease in the metabolic rate and showed that in rabbits that survived adrenalectomy, a temporary increase in metabolism occurred approximately a week after adrenalectomy. From a few studies that have been made of the metabolism in Addison's disease it seems evident that the metabolic rate is reduced in this disease.

Whether these changes are due to the medulla or to the cortex of the adrenal glands has not been definitely established. Aub, Bright and Uildil (unpublished data) showed by removing the adrenal glands of cats that had been made toxic with thyroxin that the metabolic effects of the thyroid and adrenal glands may be independent. Since the metabolism did not return to its original level after adrenalectomy it is demonstrated that thyroxin may itself keep the rate of metabolism high. Maine (59) has shown that the injection of adrenalin may increase the metabolism even when the thyroid has been removed, and, therefore, that the effects of adrenalin may be independent of the thyroid. From these experiments it seems clear that adrenalin and thyroxin exercise mutually independent influences in increasing the metabolic rate. Here, then, are two possible mechanisms for increasing the metabolism: adrenalin, which acts quickly and for minutes only, and thyroxin, whose effect is sluggish in onset and lasts for days. These facts suggest that there may be a similar regulatory control of the metabolic rate by the two corresponding endocrine glands. In another paper this theory will be fully discussed.

SUMMARY

At present the one accurate test which indicates the activity of the glands of internal secretion is the determination of the basal metabolic rate. The activity of the thyroid gland affects this most markedly. Other tissues in the body exert some influence upon the rate, but the variations which they produce are relatively small. The greatest is found in cases of leukemia, when the basal metabolism is much above normal. In anemia there is a normal or very slightly elevated metabolic rate. Removal of the gonads often causes the metabolic rate to fall and recent investigation suggests that this may be due to some interrelation with the thyroid. Work on the pituitary suggests that hypersecretion of the anterior lobe may cause a slight rise of metabolism, although this fact is not yet well established. The adrenal gland probably has a greater effect on the metabolic rate than is generally believed. As yet this is not thoroughly explained. When the adrenals are affected, as in Addison's disease, or when both adrenal glands are removed, the metabolism is low. Injection of adrenalin is followed by a rapid increase in

the basal metabolic rate This and other unpublished data have led to the theory that the metabolism may be regulated by two mechanisms, by the adrenals for rapid variations in rate, and by the thyroid gland for more sluggish but more important changes

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Book Reviews

VERHANDLUNGEN DER ZWEITEN TAGUNG UBER VERDAUUNGS—UND
STOFFWECHSELKRANKHEITEN Berlin, 1921 Verlag von S
Karger

This book contains the lectures and the discussions held at the second German Congress for Diseases of the Gastrointestinal tract and of Metabolism. The first three lectures on duodenal ulcer are of no endocrine interest. The fourth is an excellent review by Prof Richter of Berlin on "Diabetes during the war." The author, though quite agreeing with those warning against over-feeding, points out that during recent years some medical men exaggerate on the other side and let their patients starve. The discussion, following this lecture, will prove useful not only to specialists, but still more to the general practitioners. The fifth lecture by Prof Biedl on Inner secretions and Gastro-intestinal diseases has appeared in this Journal—J K

BIOLOGIA DELLA VITA EMOTIVA (BIOLOGY OF THE EMOTIONAL LIFE)
Vito Maria Buscaino, Bologna, 1921, Ed Nicola Zanichelle

Prof Buscaino attempts to show, through experimental data, that bodily changes are not caused by emotion, but instead provoked by the same external phenomena that arouse the emotion. From a minute analysis of the so-called somatic manifestations of the emotions, he states, three general laws can be deduced. Emotion, objectively considered, results in a complex of variations, in the innervation of the striped muscles, in the parasympathetic innervation, in the sympathetic innervation, and in the endocrine system. An emotion, objectively considered, differs from another, because of the qualitative and quantitative variations in the component factors just mentioned. Certain cellular groups, with the function of which a special emotional reaction is connected, can be stimulated by peculiar chemical substances of endocrine origin, so that to a special endocrine functional variation a given emotional tonality corresponds.

A long series of experiments shows that the somatic phenomena of the emotions persist in spite of surgical or functional suppression of the brain cortex. Therefore, the somatic expression of the emotions cannot be considered as a consequence of a

subjective (cortical) variation The encephalic zone, where the centers for the emotional reflexes belong, is constituted by the gray substances around the third ventricle and the aqueduct of Sylvius (ganglia the base of the brain and mesencephalon) The psychic emotional phenomena do not arise in this zone, which rules only the somatic emotional reflexes The subjective (cortical) emotion is a consequence of these activities

Bringing these principles into the pathologic field the problem regarding the genesis of morbid emotionalism becomes a problem of physiology, not of psychology We call a subject "emotional" whose subcortical centers of the vegetative affective zone are hyperexcitable Without excepting pathologic and toxic factors, the causes of this hyperexcitability are regarded as of chemical or endocrine origin

Emotional shock in an emotional subject arouses a very complex play of reciprocal actions and reactions between these centers and the periphery, especially in the endocrine ground, absolutely without the psychic field, and the consequences are nervous and mental disturbances

Through an identical mechanism the psychic and nervous phenomena of hysteria and nervous shock are consequences, revealing to us the apsychic subcortico-vegetative-endocrine complex, which succeeds in dominating the mentality of the subject

The biologic conception of the emotional life may throw light on the nature of the mental disturbances in dysphrenia, dysthymias and schyzophrenias and on the pathogenesis of dementia precox. This would be caused by an organic lesion of the vegetative-affective centers and of the cortico- and subcortico-cortical association paths —G V

DALLA MEDICINA ALLA SOCIOLOGIA (FROM MEDICINE TO SOCIOLOGY)

Nicolò Pende, Palermo, 1921

The monograph is divided in two parts 1, Endocrinology and Psychology, and 2, Vital Unity in Pathology The first part, based on the different types determined by the predominant influence of one or another of the endocrine glands on the organism, deals especially with the mental and emotional differences shown by the various endocrine constitutions The thyroid conditions quick mental reactions, easy and prompt association, and an emotional, changeable character The adrenals govern the intensity of the mental (neuro-psychic) reactions, while the gonads condition a full manly development in the mental field This is shown by the contrast between eunuchs and normal men Moebius and Metchnikoff are quoted to the effect that creative

thought and artistic genius are strictly connected with the development of the male gonads. The pituitary gland is considered as conditioning indifferent euphoria, while its failure, according to the deductions of Timme, would be answerable for moral failure. Pende then relates various forms of delinquency described by Lombroso with endocrine abnormalities, as shown by corresponding somatic stigmata, and from this does not hesitate to postulate endocrine peculiarities as governing the differences of the human races.

In the second part the condition of the organism is said to be based on the correlation of its cellular differentiations. The studies of Levi are quoted on the growth *in vitro* of the cellular elements and his finding that their autonomy of growth diminishes in inverse ratio to their higher differentiation. The chemical (hormonic) stimulation accounts for the differential growth of the cells into the different organs, and the opinion of Giacomini is emphasized as regards the startling progress of the embryonal development as soon as the thyroid begins to function.

From the lowest forms of living animals, where the relative autonomy of their several elements is rather pronounced, the organic synthesis gradually increases, until it finds in man its most highly evolved expression, not even in man, however, is there absolute synthesis, as his vegetative life still preserves some autonomy. In this regard the woman and the child offer more than man an easy dissociation, and analogous ease of dissociation is also found in long exhausting disease, in puberty and in advanced age.

Some interesting examples are quoted of partial dissociation seen during the war after trifling wounds of the hand, which suddenly developed striking symptoms all along the arm, which not less suddenly gave way at the section of the sympathetic fibres of the limb.

By following all the impressions brought to our subconscious field through the sympathetic system we may find the reason for the many different emotional conditions, which could not be explained without the knowledge of the work of the sympathetic in relation to the endocrine glands.—G. V.

THE GLANDS REGULATING PERSONALITY. A STUDY OF THE GLANDS OF INTERNAL SECRETION IN RELATION TO THE TYPES OF HUMAN NATURE. Louis Berman, New York, 1921. The Macmillan Co., 300 p., 8°

Considered as a piece of enthusiastic exposition, this book is one of the most engaging ever written in the field of endocrinology. After an introductory section dealing with adapta-

tion in relation to psychology, the author turns to endocrine physiology. Here, the instincts of the artist as distinguished from the scientist are unmistakable. Both by omission and by commission the evidence is "adapted" to the necessities of unity and balance.

For example, Cannon's theory of the emergency function of the adrenal medulla as a factor in integrative reactions, is magnified into a theory that Cannon himself has emphatically disclaimed, namely that adrenal discharge determines the reactions characteristic of strong emotion. This distorted theory thenceforth figures as a fundamental conception. The observation that the emotional reactions in question can be evoked after adrenal ablation, is ignored.

The pineal fares no better. The outstanding evidence as regards this gland is (1) Tumors of the pineal cause precocious development (possibly by mechanical effect on contiguous nervous structures), (2) Pineal feeding causes precocious sexual and somatic development, sexual depression, or no effect, depending upon what author is consulted, (3) Pineal extirpation when performed by a skilled surgeon, such as Dandy, produces no effects, presumably because no important brain structures are injured. In the face of this evidence the author manages to reach the conclusion that the pineal controls the onset of puberty.

The thymus, which also can be completely extirpated by a skillful surgeon with no perceptible effect on the subject, becomes another important regulator of sexual development. Despite the admission that "we are a good deal at sea," "Clinical observations"—nature not stated—"emphasize that in childhood it is the chief brake upon the glands of internal secretion." This supposition is supported by the often quoted statement that the thymus reaches its greatest development at puberty. As a matter of fact this structure is much more "developed"—in comparison with the body weight, which is the essential relation—in infancy, and constantly recedes as puberty approaches, ceasing its growth when that of the rest of the body ceases.

In the discussion of the pituitary its assumed relationship to sex phenomena is emphasized despite the fact that careful researches in the laboratories of Camus and of Cushing have shown that in all probability the sexual perturbations formerly ascribed to pituitary injury are due to lesions of the neighboring brain structures.

After establishing a "physiological" background the author soars into a bizarre realm of psychologic superendocrinology. One reads many such things as "Internal secretion traits are inherited and variations in heredity are essentially the structural representations of the resultant of a parallelogram of forces exerted by each of the parental propotent glands." Some pas-

sages, however, are more lucid. One learns for instance that the complexion of his neighbor's wife differs from that of her ebony cook simply because the wife has a more efficient pair of adrenals. By the same token it would seem that a victim of Addison's disease should be regarded as a negro! Such strained deductions from analogy are frequently found not only in the book under discussion but in the writings of others who would relate anthropology and endocrine science.

In numerous instances the logic of the book will not bear analysis. Post hoc arguments are frequently employed, concomitance is treated as equivalent to causality. Dubious inferences are given the coloring of fundamental postulates. But by the use of hyperbole and of figurative diction the fallacies are skilfully thrown into the background.

With how much originality the author should be credited is difficult to determine. The ideas of Crile, Rogers and Keith are freely utilized, and readily recognized as such. Those familiar with the Italian literature will recognize also numerous conceptions previously developed by Buscarno and Pende. Considering, however, the present volume of the literature on speculative endocrinology any new theoretical conception could hardly be expected.

The work as a whole impresses the reviewer as an unfortunate piece of futility. No amount of ingenuity or enthusiasm can change the fact that we are largely ignorant of endocrine fundamentals. Pasteurs are much needed but for a Darwin, even a competent one, the time is not yet ripe. The book no doubt will command a wide circle of readers, both on account of its sensationalism and the skill with which it is written. But that it will make any lasting impression upon psychologists, to whom it is particularly addressed, is doubtful, they are trained in logic as a matter of routine. To well read endocrinologists it will be but a further addition to the list of precocious interpretive dissertations to which they have perforce had to become accustomed. That it should be taken by anyone as an exposition of present day endocrinology would be deplorable.—R. G. H.

Abstract Department

A case of **ACHONDROPLASIA** (*Zur Kasuistik der Achondroplasie*)
Solotuchen, Munchen med Wchnschr, 1921, 68, 1539

A very short note on a child of 4 with achondroplasia, which, according to the author, is due to an endocrine dysfunction—J K

The autonomic nervous system and **ADENOIDS** (*Le système nerveux végétatif chez les adénoïdiens*) Ferreri (G), Ann d med navale e coloniale (Roma), 1921, 2, — (No 3)

Patients having adenoids show diminution in all their vital functions, and in this condition it is interesting to study their endocrine-sympathetic system. The action of adrenin and of atropine as well as the oculo-cardiac reflex indicate that such patients are sympathetonic. Sometimes one notes following tonsillectomy, a rapid loss of weight, together with enlargement of the thyroid gland, palpitations, gastric disorders and tachycardia—the whole amounting to a Graves' syndrome—Presse méd, 1922, 32

The influence of **ADRENIN** on the growth of tadpoles (*Ueber den Einfluss des Suprarenins auf das Wachstum der Kaulquappen*)
Bilski (F), Arch f d ges Physiol (Berlin), 1921, 191, 108-127

Adrenin has a growth-promoting action on tadpoles. A slight concentration is essential. Adrenin solutions, slightly changed through oxidation, are still effective—A T C

The action of **ADRENALIN** on the gastro-intestinal tract (*L'action de l'adrenaline sur le tube gastrointestinale*) Binet (L), Presse Med (Paris), 1918, 26, 407-408

From a study of the literature Binet concludes that experimental medicine has furnished evidence of digestive disturbances due to adrenal insufficiency. Among these are gastric ulcers, and vascular, secretory and motor disturbances.

Injection of **ADRENALIN** in an infant (*Adrenalininjektion bei einem Saugling*) Bliebung, Deutsche med Wchnschr (Berlin), 1922, 48, 47

In an infant cardiac arrest occurred during narcosis. Two-tenths cc of a 1/1000 solution of adrenalin was injected into the heart with splendid success—J K

Experimental modifications of the distribution of urinary nitrogen by the subcutaneous injection of **ADRENALIN** (*Modifications*

expérimentales de la repartition de l'azote urinaire par injection sous-cutanée d'adrenaline) Brel (J), *Compt rend Soc de biol* (Paris), 1921, 85, 1057-1058

Rabbits in a good state of nourishment and normal alimentation, when injected subcutaneously with adrenalin, show a constant rise in nitrogenous relations and often a slight rise in the relation of amino nitrogen to total nitrogen. The same is often true of a fasting animal, but not always, during prolonged fasting there may be a fall of nitrogenous relations, and a slight amino-aciduria which persists until death. Animals allowed to fast, and then fed, show notable but transient disturbance of nitrogen distribution. Contrary to Noel Paton, it appears that adrenalin acts favorably on ureogenesis. Nitrogen exchange becomes more perfect because adrenalin stimulates the amino acid function of the liver.—T C B

ADRENALIN in hyperglycemia. Brosamlen, *Deutsch Arch f klin Med* (Leipzig), 1921, 137, 299-310

Adrenalin, when injected in normal persons, always causes hyperglycemia. Glycosuria is not so constant. The author only found it in a case of Graves' disease, a case of adiposity, a case of serious tuberculosis and a case of leukemia. The glucosuria began about 3 hours after the injection, reached its height in 2 hours and never lasted longer than 11 hours. The hyperglycemia begins ± 10 minutes after the injection, reaches its maximum in 1 hour, after 2 or 3 hours a slight hypoglycemia can be found. The changes in sugar metabolism begin much later than the change in blood pressure or the disagreeable feelings of the patient. In Graves' disease the hyperglycemia is more marked than in healthy persons. In one case of myxedema the amount of blood sugar showed only a small increase. In diabetes there are different reactions. In some patients the blood sugar shows only a slight increase after the injection of adrenalin, in others it first sinks to a real hypoglycemia and then slightly rises, while in a third group of patients an enormous rise. The blood sugar shows only a slight increase after the injection of make a differential diagnosis between pancreatogenic and neurogenic diabetes.—J K

Considerable augmentation of the reaction to tuberculin by addition of ADRENALIN, and the antagonistic action of quinine and other substances (*Augmentation considérable des réactions à la tuberculine par addition d'adrenaline et action antagoniste de la quinine et d'autres substances*) Bouveyron (A), *Compt rend Soc de biol* (Paris), 1921, 85, 834-836

The addition of adrenalin to tuberculin (from Institut Pasteur) causes a marked augmentation of the skin reaction. Whereas in the control there is erythema or a papule of about 4 mm in diameter, in the tuberculin-adrenalin test the papule is livid red and 9 mm in

diameter It is painful and lasts for some days On the other hand, quinine, antipyrine and pyramidon are antagonistic, and reduce the reaction to tuberculin —T C B

Studies on the conditions of activity in endocrine glands VI
Further observations on the denervated heart in relation to **ADRENAL** secretion Cannon (W B) & Rapport (D), Am J Physiol (Balt), 1921, 58, 308-337

Further experiments to prove that the denervated heart is an indicator of adrenal secretion, and that the residual increase of heart rate after adrenal ablation is not due to rise of arterial pressure, nor to changes of venous pressure, nor to improvement of poor circulation, nor to warmer blood coming to the heart from the abdominal organs, nor to the activity of accessory adrenal tissue The paper should be read in the original —T C B

Studies on the conditions of activity in endocrine glands VII The reflex center for **ADRENAL** secretion, and its response to excitory and inhibitory influences Cannon (W B) & Rapport (D), Am J Physiol (Balt), 1921, 58, 338-352

It has been shown that the adrenal medulla is subject to reflex stimulation Two questions present themselves Where is the reflex center? Can the secretion be inhibited, and is the mechanism central or peripheral? By suitable transections of the brain stem the authors were able to trace the reflex center for adrenal secretion to the floor of the fourth ventricle, immediately behind the corpora quadrigemina They were able to get an increase of rate in the denervated heart by stimulating the sciatic or brachial after removal of the posterior colliculi, but a section 2 mm farther back completely abolished the reflex When the corpora quadrigemina and all parts anterior to them are removed, stimulation of the central end of the vagus, or of the depressor, will cause a slowing of the denervated heart by as much as 24 beats per minute This slowing does not occur if the section is made 2 mm back of the corpora If reflex adrenal secretion is maintaining the denervated heart at a faster rate, central vagus stimulation will diminish the rate The conclusion is that the reflex center for adrenal secretion at the upper edge of the fourth ventricle is subject to both excitatory and inhibitory influences —T C B

Contribution to the study of lymphogenesis Lymphagogue action of **ADRENAL** preparations and of lymphatic extracts (*Contributo allo studio della linfogenesi Sull'azione linfagoga dei preparati surrenali e degli estratti linfatici*) Chistoni (A), Arch di Fisiol (Florence), 1921, 19, 101-121

Extracts of lymphatic ganglia, injected in moderate doses intravenously into dogs produce a distinct increase of lymph flow

from the thoracic duct, the lymph possessing increased density, molecular concentration, viscosity, and electrical conductivity, and yielding increased dry residue and ash. These results are in agreement with modifications of the cellular activity. Large doses produce passage of blood and hemoglobin from capillaries to the lymph stream, and simultaneously a rapid diminution of lymph flow. Adrenal preparations also produce an increase of lymph flow, but the lymph is more dilute, with corresponding diminished density, dry residue, etc. The phenomenon is due primarily to a filtration process, hence adrenal preparations belong neither to Heidenhain's first nor second group of lymphagogues. Lymphatic gland extracts belong to the first group —A T C

ADRENALIN-lymphocytosis as a test of splenic function (*Die Brauchbarkeit der Adrenalinlymphocytose zur Funktionsprüfung der Milz*) Frey (W) & Hagemann (E), *Ztschr f klin Med* (Berlin), 1921, **92**, 450-465

Twenty minutes after the injection of 1 mgm of adrenalin lymphocytosis occurs. This is perhaps due to contraction of the spleen. The authors call the reaction positive when the absolute number of lymphocytes is increased by at least 2,500 cells. The reaction is negative when the increase is less than 1,500 cells. In all cases in which the reaction was negative there were found very marked pathological changes in the spleen. Though when the reaction is positive, changes may be present in the spleen, the follicles are always normal. This proves not only that the reaction has a practical clinical value, but that the question whether the person is "vagotonic" or "sympathicotonic" is of no importance. The lymphocytosis is not observed after removal of the spleen.

The effect of injection of ADRENIN on the capacity to form antigens Frieber (W), *Centralbl f Bakteriol [etc]* (Jena), 1921, **80**, 264-267, *Chem Abst*, **15**, 3677

Frieber of Frankfurt a M investigated the effect of adrenin injections and of unilateral epinephrectomy on the formation of antibodies. Agglutinins and hemolysins were studied. Neither procedure led to any perceptible effect. Rabbits were used as experimental animals —R G H

(ADRENAL) Variations of the vasomotor action of the splanchnic nerve (*La fonction des surrénales III Variations de l'action vasomotrice du nerf splanchnique*) Gley (E) & Quinquaud (A), *J de physiol et de pathol gén* (Paris), 1921, **19**, 355-364

In 25% of normal dogs the rise of blood pressure obtained by stimulating the peripheral end of the splanchnic does not show the stepped rise attributed to adrenalin production. In 75% it is present. But in neither case is the nature of the curve altered by

removal of the suprarenals The same applies to the cat, except that the simple rise is more common In the rabbit the double rise is never seen —Physiol Abst

(ADRENINE) The relation of the exchanges between blood plasma and tissue fluids, particularly that of the fluid of the anterior chamber of the eye and the cerebro-spinal fluid I The sugar content and the question of combined sugar (Ueber die Wechselbeziehung zwischen Blutplasma und Gewebeflüssigkeit, insbesondere Kammerwasser und Cerebrospinalflüssigkeit) de Haan (J) & Crevald (S van), Biochem Ztschr (Berlin), 1921, 123, 190-214

Rabbits were used in these studies Determinations are recorded of the sugar content of liquid from the anterior chamber of the eye, the blood plasma and the cerebro-spinal fluid Refractometric observations are also recorded The influence of the injection of adrenine on the relations was studied The results demonstrate that the glucose content of tissue liquids (aqueous humor and cerebrospinal fluid) usually is less than that of the blood plasma The opinion is expressed that the 2 former fluids can be considered as ultra-filtrates from the blood The experiments in which artificial hyperglycemia was produced by adrenalin showed that the diffusion velocity of the plasma sugar into the other liquids studied is rather rapid and of the same order of magnitude The sugar content of the aqueous humor first obtained differs from that of the blood as does the ultra-filtrate from serum The liquid which is secondarily obtained contains a large amount of plasma colloids and indeed the combined sugar Its sugar content is the same as that of plasma taken at the same time The sugar content of the cerebro-spinal fluid is much lower than that of the blood plasma and aqueous humor This difference is attributed to a greater sugar consumption by the brain The sugar content of the posterior facial vein is lower than that of the carotid blood taken at the same time and is due to a difference in the uncombined sugar from which it can be concluded that this latter is used in the tissues —F S H

(ADRENAL) The effect of intraarterial injection of adrenalin upon arterial and venous blood pressure in man (Die Wirkung intraarterieller Adrenalininjektion auf den arteriellen und venösen Blutdruck beim Menschen) Hess (F O), Arch f exper Path u Pharmakol (Leipzig), 1921, 91, 303-311

Less disturbance of blood pressure is experienced following intraarterial injection of adrenin than after intravenous administration —W J A

(ADRENIN) The influence of vagotomy upon the excretion of sugar in the kidney (Über den Einfluss der Vagusdurchschneidung auf

die Zuckerausscheidung in der Niere) Hildebrandt (F), Arch f exper Path u Pharmakol (Leipzig), 1921, 90, 142-148

After double vagotomy in the rabbit it is found that the threshold for the excretion of sugar in the kidney is quite materially lowered. The hyperglycemia was produced by injections of adrenalin. It is held that the vagus normally exerts a direct nervous influence upon the sugar-excretory function of the kidneys.—W J A

Cancer of ADRENALS Hoffman, Deutsche med Wchnschr (Berlin), 1921, 47, 1348

A woman with cancer of a bronchus got a cancer of both adrenals. No Addison symptoms developed. In this case the severe diarrhea was considered as due to the loss of functions of the adrenals.—J K

Blood acetone bodies after the injection of small amounts of ADRENALIN chloride Hubbard (R S) & Wright (F R), J Biol Chem (Balt), 1921, 49, 385-388

An increase in the acetone bodies of the blood is observed after the injection of adrenaline which does not seem to bear any relationship to changes in the blood sugar. The reaction is explained on the effect of the local restrictions in blood supply induced by the drug leading to the local production or failure of combustion of the acetone bodies. The production of these bodies is not looked on as being responsible in these experiments for the marked lowering of the alkali reserve observed.—F S H

Pharmacodynamic study of ADRENALONE Vasoconstrictor and respiratory action, secretory effects (étude pharmacodynamique de l'adrénalone. Action vasoconstrictive et respiratoire, effets sécrétoires) Jaeger (E), Compt rend Soc de biol (Paris), 1921, 85, 432-433

Adrenalone, $C_6H_5(OH)_2CO-CH_2NH-CH_3$, is an intermediate product in the preparation of synthetic adrenalin, and differs from it in having a ketone group, CO, in place of the CHOH. The author supplements the work of Loewi and Mayer, and Barger and Dale, filling in certain gaps. Experiments were made on dogs anesthetized with chloralose or chloralose and atropine. The conclusions are that qualitatively adrenalone has an action similar to adrenalin—intense vasoconstriction with rise of blood pressure, augmentation and acceleration of the heart. The effects are proportional to the dose. The intensity of its action, measured by variations in arterial pressure, is 200-220 times weaker than adrenalin. The action of adrenalone is more prolonged, due probably to the fact that it is less easily oxidized and therefore not so easily destroyed in the body. The respiratory action of adrenalone is not identical with adrenalin.

There is no long period of apnoea, but short arrests of respiration, or only relaxation, this becomes more and more intense, lasts a long time, and the respiratory movements are profound and regular Salivary and pancreatic secretions are increased, and the urine contains sugar, which lasts until the following day The urine is abundant and gives the Vulpian reaction—T C B

Pharmacodynamic study of ADRENALONE Seat of vasoconstrictor action and effects of adrenalone in the presence of various vasomotor drugs (*Étude pharmacodynamique de l'adrénalone Siège de l'action vasoconstrictive et effets de l'adrénalone en présence de diverses drogues vasomotrices*) Jaeger (E), *Compt rend Soc de biol (Paris)*, 1921, 85, 910-912

Like that of adrenalin, the seat of the vasoconstrictor action of adrenalone is the peripheral terminations of the sympathetic Adrenalone is antagonistic to the vasodilators After ergotinin, while adrenalin is exclusively hypotensive, adrenalone causes a transient hypotension, followed by the normal hypertensive effect—T C B

Intracardial injection of ADRENALIN in acute paralysis of the heart (*Intrakardiale Adrenalininjektion bei akuter Herzhlahmung*) Kneier (G), *Deutsche med Wehnschr (Berlin)*, 1921, 47, 1490-1491

In two cases of asphyxial cardiac arrest, adrenalin was injected into the heart In one case no effect was seen, in the other the patient lived 18 days—J K

(ADRENIN, PITUITRIN) The significance of calcium for the irritability of the sympathetic nerve endings in the heart (*Ueber die Bedeutung des Calciums fur die Erregbarkeit der sympathischen Herznervenendigungen*) Kolm (Richard) & Pick (Ernst P), *Arch f d ges Physiol (Berlin)*, 1921, 189, 137-143 **Inverted heart-actions of parasympathetic poisons** (*Ueber inverse Herzwirkungen parasympathetischen Gifte*) Kolm (R) & Pick (E P), *Arch f d ges Physiol (Berlin)*, 1921, 190, 108-117

(Cf Endocrinology, 5, 484) Vagus poisons (acetylcholine, muscarine, and pituitrin) produce no diastolic standstill in the isolated hearts of summer frogs immersed in a Ringer's solution rich in calcium ions Winter frogs under the same conditions behave normally The three poisons release a ventricular contracture in hearts of summer frogs previously treated with Ringer's solution containing excess of calcium and little or no potassium Atropine does not prevent the contracture (with acetylcholine) nor abolish it It is therefore independent of the vagus nerve endings It is not produced after action of ergotamine on the sympathetic heart nerves, and therefore is produced by stimulation of the sympathetic whose irrita-

bility is increased through calcium action Similar results are obtained with adrenaline—A T C

ADRENAL extirpation for epilepsy (*Exstirpation der linken Nebenniere wegen schwerer Epilepsie*) Kulenkampff, Deutsche med Wchnschr (Berlin), 1921, 47, 1543

Describes the technic of the operation—J K

ADRENIN treatment of rickets (*Behandlung der Rachitis mit Adrenalin*) Lehnerdt (T) & Weinberg (H), München med Wchnschr, 1921, 60, 1482-1484

The authors recommend subcutaneous injections of suprarenin hydrochlorid 3-4 times daily in doses of 0.2 cc of a 0.1% solution The doses must be gradually raised to 0.5 cc A calcium preparation must be given together with the adrenalin treatment The local anaemia, the palor, the influence on the pulse which are seen after the injections are of no consequence Often, even in very serious cases, a marked improvement in the psychic as well as the physical condition is seen within the first week of treatment It is advisable to treat children in this way only in a hospital—J K

(**ADRENALS**) Sensitivity of decapsulated rats to toxic substances (*Sensibilité des rats acapsulés envers les toxiques*) Lewis (J T), Compt rend Soc de biol (Paris), 1921, 85, 685-686

The susceptibility of decapsulated rats toward morphine is attenuated after a certain time In a previous note the author has affirmed that rats with unilateral decapsulation showed a diminished resistance to morphine Further observation shows that such rats resist as well as the controls—T C B

Action of ADRENALIN on the curve of hypercalcemia (*Action de l'adrénaline sur la courbe hypercalcémique*) Munoz (J M), Compt rend Soc de biol (Paris), 1921, 85, 954-955

The injection of calcium chloride intravenously in dogs is followed by a hypercalcemia which lasts for 3 to 6 hours and then falls below normal, lasting 24 hours or more Repeated injections of adrenalin do not modify the curve of serum calcium, but the total calcium did not fall below normal in five dogs thus treated, while there was a fall in the controls—T C B

The action of ADRENALIN on blood-sugar (*Ueber die Wirkung des Adrenalins auf den Blutzucker*) Petenyl (G) & Lax (H), Biochem Ztschr (Berlin), 1921, 125, 272-282

In a series of controlled experiments it was found that in man, after the subcutaneous adrenalin injection, the hyperglycemia is regularly followed by a hypoglycemia The normal blood-sugar

values show greater variability in cases of tetany than in healthy individuals, and when adrenalin is injected the hyperglycemia is usually less, eventually dies away to a hypoglycemia of greater and more lasting degree, even when hyperglycemia does not appear a hypoglycemia is induced Adrenalin hyperglycemia is hence considered to be only a partial expression of a very complicated process, the hypoglycemic stage can not be considered as a glycogen deprivation and is in certain cases independent of the hyperglycemia

—F S H

Changes in the ADRENALS in infectious diseases (Nebennieren-veränderungen bei Infektionskrankheiten) Photakis (B), Berl klin Wchnschr, 1921, 58, 1325-1326

In all kinds of infectious diseases (influenza, dysentery, typhoid, etc) all kinds of changes may be found in the adrenals Degenerations, hypertrophy as well as atrophy or necrosis are met with What changes are found depend largely upon the intensity and the duration of the disease It is possible to diagnose post-mortem the hyper- or hypo-function of the adrenals This diagnosis is more certain than the clinical one, as little is known of the function of the adrenals —J K

Antagonism between hypotensive organ extracts and ADRENALIN
L'azione antagonistica fra le sostanze ipotensive degli estratti d'organi l'adrenalina) Pugliese (A), Biochem e terap sper (Milano), 1921, 8, 65-69

Contrary to the claims of Marfori and Chistoni that in "lymphoganglin" alone a hypotensive action antagonistic to the action of adrenalin is found, the author thinks that other organs also may exert analogous action His present experiments were made with liver extract with the following results By injecting into the crural vein of a dog equal parts of adrenalin and of liver extract the characteristic action of adrenalin is strongly reduced, an enucleated eye dropped in liver extract undergoes accentuated myosis, myosis is also obtained in the eye of the dog and the rabbit with a few drops of liver extract, there is no mydriasis when adrenalin mixed with liver extract is dropped into the conjunctival sac of the dog or rabbit (For further discussion see Vincent, Endocrin, 2, 420-430)—G V

The glycogen content of the tissues of diabetic animals and the influence of ADRENALIN thereon Ringer (A I), Dubin (H) & Frankel (F H), Proc Soc Exper Biol & Med (N Y), 1921, 19, 92-97

In thirteen dogs rendered diabetic by phlorizin it was found that the muscles continued to retain a certain amount of "residual" glycogen It amounted to 0.150 per cent even after seven days of

fasting and repeated doses of the drug In five dogs it was ascertained that the residual glycogen could be completely driven out by means of adrenalin Other details of interest to students of carbohydrate metabolism are included —R G H

The effect of ADRENALIN upon respiration - Roberts (Ff), J Physiol (Lond), 1921, 55, 346-355

The common supposition that the respiratory variations caused by adrenalin are due to its direct action on the respiratory center is hypothetical This study is an attempt to clear up the matter Methods are given The conclusion is that large doses of adrenalin cause diminution and temporary arrest of respiration, with alterations of rate, and that the effect is caused by anemia of the respiratory center due to vasoconstriction There is no evidence that adrenalin causes afferent impulses from the periphery —T C B

ADRENAL insufficiency in the light of modern physiology (*L'insuffisance surrénale devant les récentes critiques des physiologistes*) Sergeant (E), Presse méd (Paris), 1921, 813-816

A general article the nature of which is indicated in the caption It is pointed out that the clinical conception of adrenal insufficiency does not imply, as many have assumed, a deficiency in adrenin secretion Such phenomena as muscular and circulatory asthenia may be ascribed largely or entirely to adrenal cortex deficiency In short, adrenin pharmacodynamics seem not to afford pertinent evidence The abstractor would add, however, that this does not necessarily exclude adrenin as a factor in "adrenal insufficiency" Recent investigators have shown that as little as 0.5 mgm of adrenin administered subcutaneously produces material augmentation of basal metabolism over a considerable period of time —R G H

EPINEPHRINURIA in normal pregnancy and puerperium (*Adrenalinuria in gravidanza e puerperio normali*) Sestini (C), Ann di obstet (Milano), 1920, —, — (No 3), Folia gynaec (Pavia), 1920, 42, 137-152, Abst , Pathologica (Genova), 1921, 13, 25

Epinephrinuria in normal pregnancy is generally very intense, especially after the third month, its intensity is in direct relation to the pigmentation Nursing puerperae show also adrenalin in the urine during the whole period of lactation, though there is no relation to pigmentation When the puerpera does not nurse her infant there is no epinephrinuria Newly born children constantly offer a negative reaction —G V

On the mode of action of ADRENALIN and of acids, against bacterial toxins (*Du mode d'action de l'adrenaline et des acides vis-a-vis des toxines bactériennes*) Tawara (S), Compt rend Soc de biol (Paris), 1921, 85, 401-402

Using mice as the experimental animals Tawara has been unable to get the results reported by Marie All the animals died from a lethal dose of tetanus toxin, notwithstanding adrenalin in varying doses was injected at different times, from immediately after injection of the toxin to 3 hours later Glucose solutions, after the method of Tachigara in rabbits, gave negative results When the toxin was mixed with adrenalin before injection, however, the mice survived after 25 lethal doses Adrenalin is acid and this is the cause of the neutralization Distilled water was made acid by HCl and boric acid, corresponding to the acidity of the adrenalin When this was mixed with tetanus toxin it had the same neutralizing effect as adrenalin Various acids were tried and the neutralizing effect was found to depend on the dissociation of H, HCl being the strongest and boric acid the weakest—T C B

Experimental dissociation of the vasoconstrictor effects and ADRENALIN secretion effects of excitation of the splanchnic (*Dissociation expérimentale des effets vasoconstricteurs et adrénalins-secréteurs de l'excitation splanchnique*) Tournade (A), & Chabrol (M), *Compt rend Soc de biol* (Paris), 1921, 85, 651-654

Excitation of the peripheral end of the splanchnic nerve causes a rise of arterial pressure, but it is a question whether it is a direct vasoconstrictor action, or indirect by causing the adrenals to secrete To solve this question an anastomosis was formed between the right lumbo-capsular vein of one dog (B), and the jugular of another dog (A) The secretion of the right adrenal of "B" is thus diverted into the circulation of "A" The carotid pressure of both animals was registered When the peripheral end of the right splanchnic of 'B' was stimulated after a latent period of eleven seconds the carotid pressure of "A" showed a rise typical of adrenalin, while hardly a second elapsed before the carotid pressure of "B" began to rise The effects lasted forty to fifty seconds after cessation of the stimulus The splanchnic, therefore, has a double action—vasoconstrictor and secretory, and in the normal subject these are merged in a common action, hypertension—T C B

(ADRENIN) Contributions to the physiology of the blood vessels
I The influence exerted by physiological fluids on the vasoconstriction produced by chemical or electrical stimuli **II** Diverse methods of action of chemical stimuli applied externally or internally to the artery Importance of the tunica interna, and functional connections between the various vessel structures (*Contributo alla fisiologia dei vasi sanguiferi I Della influenza esercitata da liquidi fisiologici sulla vaso-constrazione da stimoli chimici od elettrici II Del diverso modo di agire degli stimoli chimici applicati esternamente o internamente alle arteria Im-*

portanza della tunica interna e connessioni funzionali tra le varie strutture vasali) Vernono (Guido), Arch di Fisiol (Florence), 1921, 19, 123-162

Rabbit blood-serum increases the effect of adrenalin on the vascular system of frogs with an artificial circulation Rabbit or horse blood-serum favors and increases the contraction of rings of calf-arteries produced by adrenalin, barium chloride, or nicotin Adrenalin, brought into contact with the external surface of an isolated strip of artery, produces no contraction, even in large doses, while minimal doses produce an immediate contraction when applied to the internal surface Barium chloride produces a contraction when applied internally (immediate action) or externally (gradual action) Pericardial fluid bathing the internal surface of the artery favors the action of both adrenalin and barium It is considered that adrenalin applied externally is destroyed before it reaches the neuro-muscular junctions, while the results indicate that barium produces a mixed excitation, direct muscular, and neuromuscular

—A T C

On the excitability of the splanchnic nerve and on the movements of the intestine, after ablation of the ADRENALS (*Sur l'excitabilité du nerf splanchnique et sur les mouvements de l'intestin après l'ablation des surrénales*) Wertheimer (E) & Du villier (E), Compt rend Soc de biol (Paris), 1921, 85, 997-998

The authors believe that the excitability of the sympathetic is maintained by the secretion from the adrenals There is no doubt that the nerve possesses an excitability of its own, independent of that conferred on it by the adrenalin in the blood So far as is known these observations have not been extended to the splanchnic fibers that inhibit movements of the intestine Do these fibers preserve their activity after adrenal ablation? The experiments were made on dogs for the most part, but two cats were also used The results were clear Some hours after the operation, excitation of the nerve caused relaxation of the intestine and arrested its movements When the blood pressure falls very low it occasionally happens that the inhibitor fibers survive the vasomotor, excitation then causes relaxation of the intestine, without a rise of blood pressure It has been reported that the isolated duodenum of the rabbit after epinephrectomy contracts very feebly or not at all in Tyrode's solution In dogs and cats the contractions are just as vigorous as in the intact animal —T C B

AMENORRHEA Novak (J) & Graff (E), Ztschr f Geb u Gynäk (Stuttgart), 1921, 83, 289-313, Abst J Am M Ass (Chicago), 1921

The authors found that curetting aided in restoration of menstruation in a large number of their 111 cases of amenorrhea in

women between 15 and 39 The uterus mucosa undergoes cyclic changes even without the menstrual hemorrhage The scraps obtained by curetting show whether the mucosa is comparatively normal or atrophied, thus affording a basis for prognosis They discovered by this means in six cases a tuberculous process in the uterine mucous membrane which had never induced any appreciable symptoms —E N

Pharmacology of the AUTONOMIC system (Untersuchungen über die pharmakologische Prüfung des vegetativen Nervensystems).

Rusznayák (S), Wiener klin Wchnschr, 1921, 34, 591-592

The author examined the influence of drugs (pilocarpin) on the pupil in several persons He found that hypersensibility for adrenalin does not mean sympathicotonia There are persons who have a hypersensibility as well for pilocarpin as for adrenalin One organ may have a hypersensibility for one of these drugs whilst another organ of the same person a hypersensibility for the other drug Therefore, the words vagotonia and sympathicotonia are of no significance and do not indicate a real clinical entity The pharmacological testing of the involuntary nervous system is not reliable

—J K

Do drugs acting upon the autonomic system influence the leucocytic picture (Wirkt die pharmakologische Beeinflussung des vegetativen Nervensystems auf das weisse Blutbild)? Wollenberg (H), Ztschr f klin Med (Berlin), 1921, 92, 249-257

Pilocarpin produces in patients with a sensitive "eosinophil system" slight eosinophilia Adrenalin produces a decrease in the number of eosinophil cells in the peripheral blood together with lymphocytosis, due to migration of cells from the tissues into the blood Then an increased number of neutrophil cells is seen This is caused by an influence of the adrenalin upon the bone marrow Atropin has no influence on the blood picture It is probable that the influence of drugs on the blood picture is not caused by their influence on the involuntary nervous system, as there is no parallelism between the intensity of the change of the activity in this system and the changes in the blood picture —J K

Hypertonia and BLOOD SUGAR (Hypertonie und Blutzucker)

Härie (F), Ztschr f klin Med (Berlin), 1921, 92, 124-133

In Bright's disease with as well as without hypertonia the blood sugar, though often rather high, nearly always remains within the normal limits Real hyperglycemia is very rare The contrary is, however, seen in hypertonia without changes in the kidneys Here hyperglycemia is often met with A parallelism between blood pressure and amount of blood sugar does not exist —J K

CHOLIN as hormone of intestinal peristalsis V Experimental therapy of stomach-intestine paralysis after chloroform narcosis (Cholin als Hormon der Darmbewegung V Experimentelle Therapie der Magen-Darmlähmung nach Chloroformnarkose) von Kuhfewein (M), Arch f d ges Physiol (Berlin), 1921, 191, 99-107

A 2-hour deep chloroform narcosis produces in cats paralysis of stomach and intestinal movements with all the characteristic appearances of post-narcotic gastrointestinal paralysis seen in man. This paralysis remains complete for two hours and is still noticeable after 20 hours. Intravenous injection of cholin HCl (0.005 to 0.015 gm per kilo) has a beneficial effect on the paralysis in cats, and their general condition, the effect extending to the large intestine, and defecation being induced. When slowly injected cholin in the dosage used produces no harmful effects. The cholin-content of the cat's small intestine is not decreased by the chloroform narcosis.—A T C

CHOLINE as hormone of intestinal peristalsis III Participation of choline in the action of different organic acids on the intestine (Cholin als Hormon der Darmbewegung III Die Beteiligung des Cholins an der Wirkung verschiedener organischer Säuren auf den Darm) Le Heux (J W), Arch f d ges Physiol (Berlin), 1921, 190, 280-300

(Cf Endocrinology, 5, 247) Equivalent amounts of the sodium salts of formic, propionic, n-butyric, isovaleric, succinic, pyroracemic, and benzoic acids have been tested on surviving rabbit intestine. Salts of succinic and benzoic acids have little action, and their choline-esters not much more. The others stimulate the intestine in varying degrees, their choline-esters produce a greater or less action than that of choline itself, parallel to the action of the salts. The stimulative action of the salts on the intestine fails if choline is previously removed from the intestine by washing. Atropine antagonises the action of the choline-esters, and also, similarly, that of the salts. The results suggest the conclusion that these salts form with choline present in the intestinal wall choline-esters through the agency of a synthetic enzyme, these act more strongly than choline itself, and thus favor its action. If Neukirch and Rona's theory be correct, that certain sugars which stimulate intestinal peristalsis are broken down through the stage of pyroracemic acid, then the action of the sugar is due to the intermediate production of the choline-ester of this acid, and not through sugar-combustion setting free energy for the increased muscle-work.

—A T C

CHOLINE as hormone of intestinal peristalsis IV The influence of choline on normal stomach- and intestine-peristalsis (Cholin als Hormon der Darmbewegung IV Ueber den Einfluss des Cholins

auf die normale Magen-Darmbewegung) Le Heux (J W),
Arch f d ges Physiol (Berlin), 1921, 190, 301-310

The effect of choline on normal stomach and intestinal peristalsis in intact cats has been studied by Roentgen rays after intravenous injections of 4 to 10 mg choline-hydrochloride, amounts which the cats withstood well. Antrum peristalsis was strengthened, the waves increasing in depth and number. Passage of stomach contents into the intestine could be seen frequently. The small intestine filled more rapidly, and the stomach became empty somewhat sooner than normally. The pendular peristalsis of the small intestine was increased and followed by marked rhythmic segmentation of its contents. As a result the contents had passed almost completely into the large intestine at a time when normally the small intestine was only half emptied. There was no visible increase in the movements of the large intestine. The experiments show that when the choline content of the body is slightly increased, the choline action is increased for some hours, and the period of digestion is markedly shortened. The peristalsis remains normal in kind, there being simply an acceleration of transport of contents with no abnormal appearances.—A T C

LUTEUM EXTRACT A further report Leighton (A P), Am J Obst & Gyn (St Louis), 1921, 2, 613-619

The paper, which is along rather general lines, is based on an experience with over 300 cases in which ovarian organotherapy was employed. The author has employed thyroid in conjunction with luteum extract in some cases of menorrhagia, where pelvic disease could be ruled out. He states that "more often than not exceptional benefit has followed." He also advocates luteum extract in "dysmenorrhea of a certain type," hyperthyroidism, menopausal symptoms, sick headaches at the menstrual periods, chlorosis (together with hematinics), functional amenorrhea and hypothyroid obesity. In over half of the 300 or more women treated, the indication lay in menopausal symptoms. Of the entire number, there were not over a dozen who could not report exceptional benefit even to absolute relief. The paper, it will be seen, is of a decidedly optimistic tone, the indications for the organotherapy being more often empiric than pharmacodynamic.—E N

Action exercised by the CORPUS LUTEM on the maturation of follicles and on rut in the rabbit (Action exercée par le corps jaune sur la maturation des follicles et sur la chaleur de la lapine) Nielsen (F), Compt rend Soc de biol (Paris), 1921, 85, 614-615

From experiments in extirpating the corpora lutea in various sexual periods the conclusion is drawn that, admitting that development and maturity of the follicles is not without importance in the

production of rut, it represents only one factor in a complex, in female mammals—T C B

CORPUS LUTEUM extract in the vomiting of pregnancy Quigley (J K), Med Rec (New York), 1919, 95, 982

This is a very brief report of 17 cases Twelve were permanently benefited, and 4 were benefited with later relapse In these the author believes that not enough of the extract was given There was one complete failure The average number of doses was 7 The preparation used was in the form of 1 cc ampoules, containing 0.2 mg of desiccated gland substance—E N

Ova, CORPUS LUTEUM, menstruation cycle and the genesis of myoma (Primat der Eizelle, Corpus luteum, Menstruationzyklus und Genese der Myome) Seitz (L), Arch f Gynäk (Berlin), 1921, 115, 1-14

A dissertation the conclusions of which are that the theca-lutein cells and the follicular cells have according to their origin and function a high degree of individuality and grow and increase after the expulsion of the ovum from the follicle independently of the egg by virtue of their inherent energy, and freed from the raised intra-follicular pressure, form the temporary internal secretory gland of the corpus luteum The cells of the corpus luteum, when the ovum is not fertilized, live from 14 to 20 days after the follicular rupture They condition the ovarian and menstrual cycles The corpus luteum and the premenstrual swollen uterine mucosa induced by its activity, have an indifferent period of from 14 to 20 days duration, which is independent of the life, death or fertilization of the ovum Ovarian hormones are considered in the etiology of myoma—F S H

The liver in DIABETES MELLITUS Bate (R A), Am Med (N York), 1918, ns 13, 220-226

This article is based upon a reading of endocrinologic literature, much of it of questionable variety, and not upon original researches The author tosses about statements concerning the liver, pancreas, parathyroids, hypophysis, adrenals, spleen, hormones, etc, with all the assurance of an experienced juggler He passes from general and sometimes fantastic premises to the most startling conclusions with the dexterity of a prestidigitator, so that it is not always possible to comprehend the inner mechanism of his syncopated syllogisms—J P S

Observations on the blood fat in DIABETES Blatherwick (N R), J Biol Chem (Balt), 1921, 49, 193-199

A study of blood fat in relation to the fat in the diet shows that subjects of mild and moderate diabetes are apparently able to utilize

satisfactorily large amounts of fat, as indicated by constancy of the blood fat level and by the absence of acetone bodies in the urine
—F S H

Certain aspects of DIABETES Brown (W L), St Barth Hosp J (London), 1918-1919, 26, 104-106

A brief review with no new data —F S H

The value of saccharin as a food in DIABETES Burge (W E), Med Rec (N York), 1918, 94, 1071-1072

Burge determined the effect of feeding saccharin to dogs rendered diabetic by pancreatectomy. This feeding caused an increase of from 42 to 49 per cent in the catalase present in the blood. Similar results were obtained in human subjects suffering from this disease. Burge, therefore, believes that saccharin, in addition to being a sweetening agent, serves to facilitate oxidation and may be positively helpful in diabetes, in which oxidation is defective.

—J P S

Experimental foundation of the treatment of DIABETES by physical exercise (Die experimentellen Grundlagen einer Arbeitstheorie des Diabetes) Bürger (H), Therap Halbmonatsh (Berlin), 1921, 35, 622-628

The author found that physical work in healthy individuals causes a lowering of the blood sugar. The lowest content was found \pm 3 hours after the work was finished. The diminution is often preceded by an increase which may be 38% of the normal blood sugar. When dextrose is injected in normal individuals much less is excreted in the urine during work than during rest. It is very remarkable that if during some days a diet without carbohydrate is given physical work causes a very marked hyperglycemia. The intensity of all these reactions largely depends upon the irritability of the nervous system. The reaction is more intense when the patient is not used to the work. By systematic exercise it gradually becomes less marked. A systematic treatment of diabetes with exactly measured muscular exercise may be useful —J K

Gangrene of the limbs in DIABETES (La gangrène des membres chez les diabétiques) Ducassy (M), Thèse de Paris, 1921

In some cases of gangrene in diabetes the cause is a bacterial infection the extreme severity of which is caused by the large quantity of sugar in the tissues. There are, however, many cases in which the pathological changes are identical with those seen in Bright's disease, syphilis, etc., and where it is only a matter of gangrene in a case of diabetes, and not diabetic gangrene. Only the septic moist gangrene has a definite relation to the hyperglycemia, as such —J K

DIABETES mellitus and hemorrhagic diathesis (*Diabetes mellitus und hamorrhagische Diathese*) Gorke (H), München med Wehnschr, 1921, 68, 1324

A woman of 57 developed simultaneously a diabetes and a purpura hemorrhagica which had given rise to anemia and cachexia. Treatment of the diabetes had also a good influence on the purpura. It is believed that in these cases the purpura is due to a lesion of the endothelium, produced by the hyperglycemia —J K

The duration of fatal cases of **DIABETES** (*Die Dauer der letal verlaufenden Diabetesfälle*) Heiberg (K A), Ztschr f klin Med (Berlin), 1921, 92, 76-77

The duration of fatal diabetes is much longer in elderly than in young people. It is also longer in men than in women —J K

Blood pressure in **DIABETES** (*Über den Blutdruck bei Diabetes mellitus*) Hitztenberger (K), Wiener Arch f inn Med, 1921, 2, 461

In young patients with diabetes the blood pressure is often lower than in normal individuals of the same age, in old patients it is generally higher —J K

Hypertonia and **DIABETES** (*Hypertonie und Zuckerkrankheit*) Kylin (E), Zentralbl f inn Med (Leipzig), 1921, 42, 873-877

There are two forms of hypertonia—that with and that without high capillary pressure. Krogh has shown that the arteries and capillaries have independent innervation. In young diabetics the blood pressure is generally normal, in the elderly it is generally high. Perhaps diabetes with and that without hypertonia have different endocrine origins. It is well known that in most cases of hypertonia there is no diabetes, but nevertheless, many patients with hypertonia show low carbohydrate tolerance. It has been stated that hyperglycemia is always present in hypertonia, but Kylin could not confirm this. Probably there are relations between hypertonia and diabetes though they are not known. It is remarkable that in Graves' disease, myxedema, acromegaly and in the majority of the cases of diabetes, lymphocytosis is found. This extremely theoretical article closes with the statement that lymphocytosis, low tolerance for carbohydrates, vasolability and high blood pressure have an endocrine origin —J K

A resumé of **DIABETES** mellitus Mann (R W), Canad M Ass J, (Montreal), 1921, 11, 243-245

Chemical and clinical data of five cases are included. Chem Abst, 15, 3873

Trauma and DIABETES Niemeyer (H), *Geneeskundig Tijdschrift der Rijksverzekeringsbank (Amsterdam)*, 1921, 6, 340-347

Description of a man who 14 years after a severe trauma died in coma diabeticum Nine years after the trauma the first symptoms of diabetes appeared During these 9 years the patient always had nervous complaints The insurance company refused to pay because it did not regard the diabetes as caused by the trauma After a trial in which the best Dutch medical men were heard, it was, however, decided that it was highly probable that the diabetes was caused by the trauma —J K

Simple method of determining the approximate degree of acidosis in DIABETES mellitus Rabinowitch (I M), *Canad M Ass J* (Toronto), 1921, 11, 526-528

Details of five cases in which the Van Slyke and Palmer procedure was used *Chem Abst* 15, 3873

A study of the relation between syphilis and DIABETES MELLITUS Rosenbloom (Jacob), *Am J Syphilis* (St Louis), 1921 5, 634-642

This paper contains a review of the literature and a study as to the presence of signs of syphilis in one hundred and thirty-nine cases of diabetes mellitus Sixteen of these cases presented a positive Wassermann test, a percentage of over twelve Eight of these cases presented signs of arteriosclerosis It is possible that these eight cases of diabetes are syphilitic in nature, and as a part of the arteriosclerosis there would undoubtedly be present some fibrosis of the pancreas These eight cases were subjected to intensive treatment for the syphilis, but there was no increase in their tolerance for carbohydrates This is no doubt due to the fact that the pancreatic fibrosis still exists after the treatment We may conclude, therefore, that in this series studied, sixteen cases presented positive Wassermann tests In about six per cent of the cases studied the diabetes existed as a part of the syphilitic process and in about six per cent the syphilis and diabetes existed as independent conditions

—Author's Abstract

A study on the viscosity of the blood in DIABETES (*Etude sur la viscosité sanguine chez les diabétiques*) Rousseau (C) Thèse de Paris, 1920

The author studied the viscosity of the blood in diabetes after adding sodium citrate to it to prevent coagulation When the viscosity was estimated the blood was centrifuged and the viscosity of the plasma was measured The difference between these two values is considered as the viscosity of the corpuscles In consumptive diabetes especially when coma is coming on, the viscosity of the

total blood is largely increased This is due to an increased viscosity of the corpuscles, the viscosity of the plasma remaining nearly constant The viscosity has no relation to the quantity of sugar in blood or urine —J K

Experimental GLYCEMIA and hyperglycemia in normal subjects (*Glycémie et hyperglycémie expérimentale chez les sujets normaux*) **Experimental HYPERGLYCEMIA in glycosurics and in DIABETICS** (*Hyperglycémie expérimentale chez les glycosuriques et les diabétiques*) Labbé (M), Labbé (H) & Nepveux (F), *Compt rend Soc de biol (Paris)*, 1921, 85, 397-400

Two articles, with nothing especially new Curves are given and the difference between hyperglycemia of normals and of diabetics are pointed out —T C B

DIABETES mellitus Willcox (W H), *Practitioner (Lond)*, 1921, 57, 305-321

The author calls attention to the several types of diabetes, mentioning also the Pavy variety of alimentary glycosuria associated with arteriosclerosis and hypertension, and the so-called "diabetes innocens" in which the quantity of sugar excreted in the urine bears no relation to the amount ingested Diabetes appears to be increasing in prevalence as evidenced in the mortality statistics of England and Wales Willcox summarizes Allen's views on the "pancreatic amboceptor" as related to diabetes and reminds us that despite the lack of pancreatic hormone, its administration by mouth or injection has no influence in the control of diabetes Lowering the assimilation limit for sugar or on the other hand increased carbohydrate tolerance in disease of the posterior lobe of the pituitary is referred to Disturbed carbohydrate metabolism is sometimes observed in Graves' disease, rarely even in myxedema Willcox favors the etiological importance of infections in the causation of diabetes, but has not had success in treatment with autogenous vaccines The symptoms of hyperglycemia are recorded, also those of acidosis Early recognition of the latter is urged in order to prevent diabetic coma from which recovery is rare Treatment is then carefully discussed, particularly referring to the methods of Allen and Joslin

—H L

Observations on the treatment of DIABETES INSIPIDUS with infundin Bullowa (J C M), *Med Rec (N York)*, 1918, 93, 127

This is a brief report of a case of diabetes insipidus in a boy of fifteen When the salt intake was diminished, the amount of urine was reduced and the specific gravity of the urine increased, but it never rose above 1007 Hypodermic injections of 1 cc of pituitrin caused a marked concentration of the urine about two and one-half to three hours after the injection The specific gravity of

the urine usually rose to 1020, with a marked diminution in the quantity of water excreted. The subsequent fall in specific gravity was gradual. The effect of the dose, as measured by the increase in specific gravity, was about seven hours. There was no acute thirst until fourteen to sixteen hours after the administration of the pituitrin. A single dose induced, in about two minutes after its injection, marked pallor of the skin, dilatation of the pupils, and headache, accompanied by a slowing of the heart and a fall in blood pressure. The pallor of the skin lasted about fifteen minutes and the fall in blood pressure about forty-five minutes. The administration of pituitrin and of minced gland by mouth was without effect.

—J P S

The results of the operative treatment of DYSMENORRHEA (Die Resultate der operativen Behandlung der Dysmenorrhoe) Forssner (H), Upsala Läkareförenings Förhandlingar, 1921, 26, Sept 1, No 5-6, Abst Jour Am M Ass (Chicago), 1921, 77, 1458

Forssner admits that an unstable nervous system and tendency to emotionalism are important factors in painful menstruation. In the 153 cases of dysmenorrhea for which he was consulted during the last ten years, and for which no appreciable cause could be discovered, he found that in 88 these subjective factors were responsible for the disturbance to such a degree that by training the patient in self-control and will-power the dysmenorrhea was often practically cured. In 65 other cases he found that while this helped, yet something more was needed. The premenstrual congestion of the uterus mucosa seems to be the cause of the pains, as the uterus is too narrow, and in seeking to correct this, the uterus contracts, as with a labor pain. Among the arguments advanced to sustain this view is that the first childbirth usually puts an end to the dysmenorrhea permanently, as the uterus gets stretched. Another argument is that patients in labor with their first child have told him that the labor pains were just like those they had had in the painful menstruation. His intervention is therefore merely to stretch the uterus and cervix, aiming to induce contractions as with labor. He dilates the cervix with Hegar bougies. With young girls this cannot be done with more than a No 10 or 12. Then he tampons the cavity of the uterus as completely as possible, and leaves it for forty-eight hours, which often induces quite painful contraction of the uterus. The tampon is then removed and a larger bougie introduced up to No 20. He then investigates the uterus with the finger and usually follows with curetting. Then he tampons anew and leaves the tampon for another forty-eight hours. He has never had any mishaps with this technic and never infection. If the patient objects to this treatment he never tries to urge her. In 54 of the 58 cases in which he applied it, 46 per cent have never had

any dysmenorrhea since In 34 per cent of the cases there is still a little pain at menstruation, but nothing to compare with the previous disturbances, and the women keep up and about, which was never possible before About 20 per cent of the total say that the dysmenorrhea is the same as before or the improvement was only for a few months The interval since has been from ten to seven years in 14 and from one to five years in others If disturbances return it might be possible to banish them anew by repeating the procedure The other women in his list passed through pregnancy not long after and are omitted from his figures In conclusion he remarks that this proportion of 80 per cent cured or immeasurably improved commends this harmless method for treatment of severe dysmenorrhea (In German) —E N

A case of general DYSTROPHY (Vorstellung eines Falles von eigenartiger allgemeiner Dystrophie) Yamin, München med Wchnschr, 1921, 68, 1540

The patient was a girl of 9½ with sexual precocity, well developed sexual organs, good intelligence, spasms in fingers, arms, feet and legs, hypoplasia of the skin (with dirty spots), and hypoplasia of bones and muscles The liver, spleen and lymph glands were much enlarged, the heart, thyroid and hypophysis (by radio-scropy) also Perhaps the clinical diagnosis should be pineal tumor —J K

The influence of ENDOCRINE preparations on gaseous metabolism (Die Wirkung der aus endokrinen Drüsen hergestellten Präparate auf den Gaswechsel) Arnoldi (W) & Leschke (E), Ztschr f klin Med (Berlin), 1921, 92, 364-375

The authors studied the influence of thymin, hypophysis (pars, anterior and posterior), thyreoidin, adrenalin, and luteoglandol on gaseous metabolism The influence was found to be not constant even in the individual subject When a large dose of one of these substances is given carbohydrate metabolism is first increased, but the fat and protein metabolism is also raised —J K

ENDOCRINE functions and the digestive apparatus Barker (L F) Med & Surg (St Louis), 1918, 2, 655-678

An extensive critical analysis and classification of the role of the endocrine organs in digestive functions From the summary the conclusions can be made that the outstanding features of such relations are the diarrhea and accelerated metabolism in Graves' disease, the constipation and retarded metabolism of myxedema, the enamel defects and disturbances of calcium excretion in parathyroid insufficiency and the relation of gastric and duodenal dilatation to tetany, the large medial incisors and long intestine in status thymo-lymphaticus, the relation of the anterior lobe of the hy-

pophysis to obesity and splanchnomegaly and of the pars intermedia to diabetes insipidus and its accompanying thirst, the relation of the pancreas and the chromaffin system to the mobilization of glucose, and the hormonal significance of secretin, gastrin and anti-thrombin produced within the digestive tract—F S H

The role of the ENDOCRINES in common medical diseases Blumgarten (A S), *Med Clin of N Am (Phila)*, 1921, 4, 1437-1507

The author presents numerous cases showing endocrine manifestations in common medical diseases. The evidence is based on clinical data, basal metabolism tests and all other necessary laboratory examinations. The role of the thyroid and adrenal apparatus in gastric neuroses is first considered. Endocrine syndromes fall in the following categories: (1) Frank endocrine syndromes, (2) *Forme fruste* types of classical syndromes occurring in two forms—either a mild type or as a type with dominant symptoms in other viscera, (3) Classical manifestations of immune reaction in infections, or as the initial onset of the infection, (4) Endocrine disturbances in functional diseases as a result of disturbance in the endocrine regulating mechanism.

Gastric neuroses include (a) Cases showing marked or slight evidence of hyperthyroidism or thyroid deficiency, (b) Cases with gastric symptoms as the earliest manifestation of hyperthyroidism and thyroid deficiency which only later manifest themselves, (c) Cases showing a domination of the thyroid or the adrenal glands in the physiology of the patient—the so-called “thyrotropes” and “adrenotropes”. The author treats functional gastric neuroses as he would an underlying endocrine disturbance. Hyperthyroidism is treated by physical and mental rest, and the usual remedies for this condition. He has used adrenal cortex, however, for an underlying adrenal cortical insufficiency, on the basis of clinical data, for the relief of the hyperthyroidism, with excellent results in the improvement of the gastric symptoms and the hyperthyroidism. (This is the first report of the use of adrenal cortex in hyperthyroidism.)

The following cases are presented. The underlying thyroid disturbance is established on the clinical data of the basal metabolism determinations: (1) A case beginning with gastric symptoms after influenza developing frank exophthalmic goitre a year later. (2) Hyperthyroidism beginning with gastric symptoms after the emotional shock of a hold up and developing frank hyperthyroidism symptoms months later. (3) Hyperthyroidism beginning with gastric symptoms diagnosed as an ulcer and operated upon but with no ulcer found a year later frank hyperthyroidism developed. (4) A case of *forme fruste* type of thyroid deficiency. (5) Three cases of functional gastric neuroses occurring in a thyroid-dominant type of patient. (6) Functional gastric symptoms in a male patient.

of the dominant adrenal type In these cases the existing gastropotosis is a constitutional stigma, not the cause of the symptoms

The relation of the pituitary to adolescent epilepsy and nocturnal enuresis is then considered A few points are emphasized The small contracted pelvis is a pituitary manifestation Undescended testes occur in pituitary deficiency, indicating deficient gonadal development in association with pituitary deficiency The frequency of nocturnal enuresis and fits occurring in adolescence in association with other frank pituitary manifestations, or with a forme fruste type is pointed out Three cases are presented (1) Acromegaly with subsequent Frohlich manifestations and genital atrophy, occurring in adult life, with erosion of the sella turcica, (2) A case of classical Frohlich syndrome with epileptic fits, (3) Three brothers with hereditary dyspituitarism, with marked genital atrophy, the mother of whom showed similar symptoms of dyspituitarism—Author's abst (abbreviated)

On the diagnostic and therapeutic importance of the ENDOCRINE ORGANS in the pathology of the stomach (Ueber die diagnostische und therapeutische Bedeutung der Blutdrusen fur die Magenpathologie) Boenheim (F), Deutsche med Wchnschr (Berlin), 1921, 47, 1256

The excretion of chlorine takes place as well through the kidneys as through the stomach In diseases of the stomach this excretion may be just as well disturbed as in diseases of the kidney The thyroid mobilizes chlorine The exophthalmos, wide pupils, increased perspiration, nervous irritability and other symptoms of Graves' disease are also found in tuberculosis and in diseases with hyperacidity of the stomach, such as ulcer ventriculi This is, of course, not a proof that this condition is due to an abnormal function of the thyroid It is, however, a fact that after injections of thyroid extracts the acidity of the stomach is raised Pancreas, hypophysis and gonads seem to have the same effect on the stomach, though much less is known about them The pineal seems to have no influence The thymus and the adrenals have an opposite influence The thymus hormone, if there is such, has a most splendid influence in many cases of hyperacidity It diminishes the amount of chlorine in the blood and the secretion of the stomach and is specially indicated in cases with symptoms of hyperthyroidism The same may be said for the adrenals—J K

Skin diseases and the ENDOCRINE ORGANS (Ueber Zusammenhang von Dermatosen und innerer Sekretion) Brock (W), Deutsche med Wchnschr (Berlin), 1921, 47, 1420-1421

The author states that there exist relations between the thymus and the cutaneous epithelium He obtained splendid results in

psoriasis, lichen ruber planus and verrucosis and ichthyosis with exposure of the thymus to x-rays. He thinks that injections of preparations of thymus probably have the same effect, though he has not hitherto had much experience with this treatment —J K

(ENDOCRINE ORGANS) Studies on ENDOCRINE facies (*Estudio da facies em endocrinologia*) Diaz (A), *Revista dos Cursos* (Porto Alegre), 1921, 7, 214-235

This is a clinical study illustrated with numerous photographs. It deals with the different varieties of facial expression and treats of their importance in the diagnosis of endocrine disturbances

—B A H

(ENDOCRINE ORGANS) A remarkable disease cachexia and pluriglandular insufficiency of the glands with external and internal secretion (*Über ein eigenartiges Krankheitsbild Kachexie und polyglanduläre Insuffizienz der Drüsen mit ausserer und innerer Sekretion*) Edelmann (A) & Saxl (G), *Wiener Arch f inn Med*, 1922, 3, 227-234

Three interesting cases are described (1) A woman of 52 had glaucoma, atrophy of the tongue and acidity of the stomach, fatty stools, no polyuria, no bradycardia, and defective intelligence as seen in myxedema. At autopsy there were found atrophy of all organs, but especially of the thyroid, pancreas and adrenals, together with osteoporosis. (2) A woman of 51 showed loss of hair, stupidity as in myxedema, sclerodermia, atrophy of the tongue, fatty stools and anacidity. At autopsy atrophy of all organs but especially of the thyroid and pancreas, with osteoporosis was found. (3) A man of 51 showed edema of the legs, fatty stools, loss of hair, atrophy of the tongue and anacidity of the stomach. Post-mortem there were found marked atrophy of the thyroid and slight atrophy of the pancreas and testicles, but no osteoporosis. Pulmonary tuberculosis was also noted. The authors believe that this association of manifestations constitute a disease entity and that it is caused only by severe injuries as starvation, infection, etc. It is perhaps possible that the normal functions of the glands with external secretion depend upon normal hormone production —J K

(ENDOCRINE ORGANS) The colloids of the body fluids (*Kolloidzustand der Körperflüssigkeiten*) Ellinger (A), *Deutsche med Wchnschr* (Berlin), 1921, 47, 1479

The viscosity of the serum is decreased by administration of caffeine, theobromin, strophanthin, adrenalin, it is increased by histamin, thymus, extract of hypophysis. Extracts of ovary or testicles, and morphine and atropine have no influence —J K

(**ENDOCRINOLOGY**) On organotherapy (Ueber Hormontherapie), Furth (O), Wien klin Wchnschr, 1921, 34, 521-522

A very short review of the indications for organotherapy with thyroid, hypophysis, adrenalin, thymus and gonads. Nothing new
—J K

The **ENDOCRINE ORGANS** and gynecology (Innersekretorische Frage in der Gynaekologie) Halban (J), München med Wchnschr, 1921, 68, 1314-1317

A good general review, without new facts —J K

(**ENDOCRINE ORGANS**) Glandular dystrophies, particularly the mono-symptomatic dystrophies (Dystrophies glandulaires et particulièrement dystrophies mono-symptomatiques) Hutinel (V) & Maillet (M), Ann Méd (Paris), 1921, 10, 198-227

"It is difficult to classify the endocrine dystrophies on both a rational and clinical basis" However, the authors divide the mono-symptomatic dystrophies into two groups. Into the first are placed the aplasias or arrests of development, and the atrophic regressions. In the second group are placed those disturbances of abnormal nutrition from which result a modification of the character, resistance form and functional value of the organ in question. It is impossible to give an adequate abstract of this very complete article in which with some detail there is given the role of the various endocrine glands in the production of the symptoms by which the above classification is arrived at —F S H

ENDOCRINE influence, mental and physical, in women King (J E), Am J Obst & Gyn (St Louis), 1921, 1, 341-349

A discussion, along philosophical and largely hypothetical lines, of the influence of the endocrine glands upon women, especially as to various phases of her psychology. The concluding line is 'Woman, with all thy glands, we love thee still' —E N

(**ENDOCRINE GLANDS**) Report of the anatomical findings in a case of pluriglandular disease [Beitrag zur Kenntnis der anatomischen Befunde bei polyglandularer Erkrankung (Insuffisance pluriglandulaire)] Landsteiner (K) & Edelmann (A), Frankfurt Ztschr f Path (Wiesb), 1920, 24, 339-353

The authors report a case and briefly review the literature. The major clinical features were as follows. Female, aged 17 years, of low-grade intelligence, well nourished, dry skin, jaundice, marked development of the mammary glands, absence of axillary and pubic hair, lymphocytosis 45%, Wassermann negative, moderate secondary anaemia, died in coma. At necropsy the pituitary measured 15x7 mm. The thyroid was small, stroma increased, with definite atrophy

of the follicles There were enlarged tuberculous bronchial lymph glands, terminal streptococcic peritonitis, high grade cirrhosis of liver with enlarged spleen Thymus present, moderately fatty Right ovary measured 4x1 cm and the left 3x1.5 cm Bony skeleton, everywhere fragile, thinned out, spontaneous fractures of the long bones The parathyroids, suprarenals, pituitary and pineal glands are described as normal—D M

(ENDOCRINE GLANDS) The growth of tissues in the test-tube under experimentally varied conditions with special reference to mitotic cell proliferation Loeb (L), & Fleisher (M S), J Med Research (Boston), 1919, 40, 509-550

The purpose of this paper is to report experiments in which the authors analyze the factors which determine the mitotic proliferation in tissues growing in culture media under experimentally varied conditions In most of the experiments kidney tissue was used A limited number of experiments were made with thyroid and parathyroid glands, testicle and ovary The parenchyma and stroma of the peripheral parts of thyroid and testicle may survive transplantation into coagulum in a test tube In both thyroid and testicle the central parts of the transplants became necrotic The colloid of the acini of the thyroid frequently disappeared in the same way as after transplantation in vivo The typical thyroid structure was maintained, and the thyroid cells sometimes showed mitoses In the testicle only scattered nuclear figures, different from the typical mitoses in other organs, were observed In the tubules the production of spermatozoa was not seen to continue in vitro While in the thyroid in the test tube the stroma perished to a great extent even in the peripheral parts, in the testicle, on the contrary, the stroma seemed to be more resistant, this is probably due to the tendency of the testicular stroma to become transformed into interstitial cells Passing oxygen through the container caused increase in the size of the preserved area in the pieces of thyroid, but not in pieces of the testicle The peripheral parts of parathyroid may likewise survive in the test tube In the case of the ovary the same kind of structures survive after transplantation into the test tube as after transplantation into subcutaneous tissue, namely, the small follicles, germ epithelium and tunica albuginea Mitotic activity was noted in the germ epithelium, but not in the follicles, in the test tube—J P S

The ENDOCRINE origin of muscular dystrophy Manney (N W), Goodhart (S P), & Clark (L P), Med Rec (N Y), 1918, 93, 128

Brief abstract of an article which appeared later in Arch Int Med, 1918, 21, 188-215—H L

(ENDOCRINE ORGANS) Anatomical and clinical study of a case of Erb-Goldflam's myasthenia gravis (*Étude anatomo-clinique d'un cas grave de myasthénie de Erb-Goldflam*) Marie (P), Bouttier (H) & Bertrand (I), *Ann Méd (Paris)*, 1921, 10, 173-184

Plates showing disturbances of adrenals, thyroid and thymus in this disorder —F S H

(ENDOCRINE ORGANS) Asthenias due to pluriglandular disorders of syphilitic origin Merklen, Devaux & Desmouliere, *Presse méd (Paris)*, 1921, 29, 14, *Abst Am J Syphilis (St Louis)*, 1921, 5, 687-688

The manifestations of syphilis are not necessarily objective and may comprise purely subjective states such as asthenia. This knowledge is naturally due to serodiagnosis. Women are especially apt to complain of an unmotivated sense of prostration, which may be continuous or intermittent and vary more or less in degree. Ordinary therapeutic resources are used in vain. The condition passes for one of nervous invalidism. The usual resources such as visiting or change of residence brings about only a transitory amelioration, and a crisis may occur in the midst of such a change. The authors do not claim to have first discovered this morbid state for it has been described as syphilitic neurasthenia. But the latter when secondary to another process is practically an organic affection. To what system then shall we attribute it? In the present state of our knowledge we are apt to think of the endocrine glands and especially the adrenals. Congenital syphilis, as shown by Hutinel, may act destructively on these bodies and set up dystrophies, hence in the acquired syphilis of the adult, something of the same nature may occur. Asthenia attends on various clinical expressions of secondary syphilis, but we are not interested in the asthenia which accompanies outspoken lesions but solely in this connection in a form which appears rather suddenly during the evolution of the disease and indicates that the virus has done some damage to one or more of the endocrine glands. The blood gives a slightly positive Wassermann reaction. Specific treatment ameliorates and if persisted in may cure —R G H

(ENDOCRINE ORGANS) Salt excretion in relation to constitution (*Versuche über Kochsalzausscheidung von konstitutionellen Gesichtspunkten aus betrachtet*) Moewes (C), *Ztschr f klin Med (Berlin)*, 1921, 92, 376-380

The author examined the excretion of NaCl, after administration of extra quantities in several persons. Amongst ten patients with a normal excretion, three had a *habitus asthenicus*, six *hyperthyroidism*, and one *hypothyroidism*. Of nine patients with an in-

creased excretion, four had a habitus asthenicus, three hyperthyroidism, two hypothyroidism. Of 12 patients with a defective excretion of NaCl, two showed a habitus asthenicus, seven hyperthyroidism, and three hypothyroidism. There is no relation between constitution and excretion of NaCl — J K

(ENDOCRINE GLANDS) Studies on compensatory and correlated hypertrophy (*Untersuchungen über kompensatorische und korrelative Hypertrophie*) Nigst (P), Schweiz med Wchnschr, 1921, 51, 155-156

Two types of work hypertrophy are distinguished (1) compensatory, as for example, the hypertrophy of the remaining portion of the thyroid after the removal of three-fourths, and (2) what he calls correlated hypertrophy, as for example, the hypertrophy of the hypophysis after thyroidectomy. While much is known of hypertrophy in general, we are still poorly informed concerning many of the finer mechanisms involved. One of these, the influence of the nervous system, is the subject of the present report in which the kidney was studied. Two groups of rabbits were used. In one, one kidney alone was removed. In the other, after removing one kidney, all nerves going to the kidney were destroyed by dissecting the renal artery and vein and ureter as free from nerves as possible, then applying pure carbolic acid followed by alcohol to destroy any remaining fibers. The compensatory hypertrophy was as rapid and as marked in the denervated kidney as when the nerves were left intact. As an example of the so-called correlated hypertrophy, advantage was taken of the suprarenal—thymus interrelation. According to Matti, the suprarenals enlarge following thyroidectomy in dogs. The author thymectomized rabbits with and without denervating (cutting the splanchnic) one suprarenal. He noted no difference in the suprarenal reaction depending on denervation and concludes that neither compensatory nor the so-called correlated hypertrophy are dependent upon nerve influences — D M

(ENDOCRINE ORGANS) Certain pluriglandular anomalous functions associated with psychopathic sexual interests. O'Malley (M), J Nerv & Ment Dis (N Y), 1918, 48, 1-35

These interesting studies accompanied as they are by many photographs are suggestive but too diffuse to be conclusive, although the author does state that there is no definite mental reaction type associated with the endocrinopathies — F S H

(ENDOCRINE GLANDS) The influence of a lack of calcium in the food on the respiratory exchange (*Untersuchungen über den Einfluss des Calciummangels in der Nahrung auf den respiratorischen Grundumsatz*) Pedotti (F), Biochem Ztschr (Berlin), 1921, 123, 272-283

Rats were kept on a calcium-free diet and an attempt was made to deplete the body of calcium by potassium feeding. The determination of the respiratory exchange showed that a lowered basal metabolism resulted from the lack of calcium. No histological changes took place in the thyroid, parathyroids or bones.—F S H

(ENDOCRINE GLANDS) *The iron man and the mind* Pound (A), *The Atlantic Monthly* (Boston), 1922, 129, 179-189

"The operating of automatic and semi-automatic machinery evolves evidence tending to show that fatigue, instead of being simply weariness from muscles stretched too much or too often, is rather a pathological condition, due to the poisoning of the system through over-secretion of the endocrine glands. Whatever the theorizing as to endocrine glands, it is probably true there is an excessive outpouring under nervous tension, when effort is prolonged beyond the normal fatigue limit. Glandular secretions, roused by an over-stressed fraction of the anatomy, spread beyond that fraction to stimulate the rest of the man into heightened activity"—F S H

The literature on the ENDOCRINE ORGANS in 1921 (Yaaroverzicht van de literatuur over de klieren met inwendige afscheiding) Stuurman (F J), *Ned Tijds v Geneesk* (Haarlem), 1921, 65, 3077-3096

A general review —J K

Clinical ENDOCRINOLOGY Timme (W), *Neurol Bull*, (N Y), 1921, 3, 3-33

This article is a lecture which embodies an interesting general exposition of some of the more important endocrine data together with the author's system of endocrine philosophy. It is not amenable to abstracting.—R G H

(GONADS) *The rôle of the nucleus in the epididymal secretion* (Sur le rôle du noyau dans la sécrétion épидидymaire) Benoit (J), *Compt rend Soc de biol* (Paris), 1921, 85, 946-948

A histological description of the cells of the epididymus, showing the conditions during the secretion from the nuclei

—T C B

(GONADS) *The over-appreciation of the puberty gland* (Die Ueberschätzung der Keimdrüse) Biedl (A), *Deutsche med Wchnschr* (Berlin), 1921, 47, 1247

Biedl is not convinced of the truth of Steinach's teachings. The organism is sexual from the beginning and the question whether a male or female individual will be formed was determined in the structure of the ovum and the spermatozoön. Every endocrine

organ has an influence on the secondary sexual characters This is especially true for the thyroid and the adrenals —J K

(GONADS) Marked lipid hyperplasia of both ADRENALS with foci of calcification in a pseudo-hermaphrodite with bilateral undescended testis and an accessory suprarenal in the right testis [Hochgradige Lipoidhyperplasie beider Nebennieren mit herdförmigen Kalkablagerungen bei einem Fall von Hypospadias penisscrotalis und doppelseitigem Kryptorchismus mit unechter akzessorischer Nebenniere am rechten Hoden (Pseudohermaphroditismus masculinis externus)] Brutschy (P), Frankfurter Ztschr f Path (Wiesb), 1920, 24, 203-240

Reports the case of a pseudo-hermaphroditic male infant, aged 17 days, with a clinical diagnosis of difficult labor, subdural hemorrhage, congenital heart defect and carbon dioxide intoxication The post-mortem examination showed a large, active thymus, normal thyroid, enlarged spleen, adrenals markedly enlarged, measuring 3.8x2.2x1 cm The surfaces of both suprarenals were nodular There were two minute accessory suprarenals in the capsule of the right kidney Uterus and vagina absent Sex glands resemble testes and measure 8x6x4 mm as compared with 10x8x7 mm of the testes of a normal 47 cm infant On the right sex gland there was a small accessory suprarenal gland The suprarenal enlargement was mainly cortical, which was very bright yellow in color External genitalia were those of a normal female infant Microscopically, no definite adrenal medulla tissue was found, the whole gland being composed of irregular large and small adenoma-like masses In places, cholesterol spaces and giant cells were found Testes and hypophysis showed no noteworthy changes Reviews literature reports of cases (1) with accessory suprarenals in genital malformations, (2) with suprarenal hyperplasia and accessory suprarenals in right testis in male pseudo-hermaphrodites, (3) with suprarenal hyperplasia and accessory suprarenals in female pseudo-hermaphrodites

—D M

(GONADS) Constitutional eunuchoidism Eichhoff, Berl klin Wchnschr, 1921, 58, 818

The patient is a healthy man of 34, rather large but of the female type The pelvis has the female form There are but few hairs on the trunk or the face The muscles are well developed The voice is high pitched The external genitalia are underdeveloped but potentia coeundi and sexual desire are normal Though he has been married seven years he has had no children A skiagram of the skull shows an extremely small sella —J K

(GONADS) The scurf of rats and its relation to Steinach's rejuvenation (Ueber die Rattenscurf und ihre Beziehung zu den Stein-

achschen Verjüngungsversuchen) Flebiger, (J), Wien klin Wchnschr, 1921, 34, 364-366

Steinach's book on rejuvenation contains many splendidly executed photographs. From these Flebiger made the diagnosis of "scurf" in Steinach's animals. Steinach himself points out that animals with lice are of no use for his experiments since they exhibit senile symptoms. Steinach does not speak about scurf, but the symptoms which he considers as senile—loss of hair on the scrotum, bald spots on the back, loss of weight, loss of sexual desire—are all symptoms of scurf. It is a well known fact that when horses are attacked by scurf they rapidly become senile. Flebiger holds that Steinach's results are probably not due to his operations, but to his cure of the scurf by proper nursing, feeding and cleaning of the animals.—J K

(GONADS) Sexual neutralization obtained by means of orchilytic and ovariolytic serum (Neutralizzazione sessuale ottenuta mediante sieri orchilittici ed ovariolittici Giuliani (R), Ann d'ig (Roma), 1920, 30, 323-326, Abst, Pathologica (Genova), 1921, 13, 542-578

The result of these experiments show how through orchilytic serum a degeneration of the testis can be obtained to the extent of hindering their very function. A microscopic examination revealed deep alteration of the parenchyma that had become granular. The seminiferous tubules could hardly be identified. Albuginea and connective tissue remained unchanged.—G V

(GONADS) Congenital idiocy (Angeborene Idiotie) Kellner, Berl klin Wchnschr, 1921, 58, 1393, Deutsche med Wchnschr (Berlin), 1921, 58, 1393, Deutsche med Wchnschr (Berlin), 1921, 47, 1511

A boy of 10 is described with extremely small generative organs. In the penis no corpus cavernosum was present and testicles could not be detected.—J K

(GONADS) Youth and old age (Jugend und Alter), Kohn (A), Wien klin Wchnschr, 1921, 34, 494

The author does not agree with Steinach's teachings. It is true that after ligation of the vasa deferentia the interstitial cells of the testis increase in number, but this is not a proof that they possess an increased endocrine function.—J K

(GONADS) Steinach's theory (Die Lehre Steinachs) Lipschutz Deutsche med Wchnschr (Berlin), 1921 47, 1247

The author is absolutely sure that the interstitial cells exert an endocrine function. He believes that the embryo is asexual and

that the development of the interstitial cells is the cause of sexual differentiation —J K

(GONADS) The so-called interstitial gland implantation To whom is the credit due? Lydston (G F), Am J Surg (N Y), 1920, 34, 77-80

The author reviews the early attempts at transplantation of reproductive glands, beginning with Berthold's work on fowls in 1849, notes the first reported transplantation in this country by Hammond and Sutton in 1912, and gives in detail his own experiments and conclusions The terms "interstitial glands" is of newspaper science origin—while the "between cells" of Leydig are supposed to secrete hormone, they are not true gland cells and transplantations are not confined to the "glands interstitielle" In 1914 the author found that part of a gland transplanted into its own tissues became in part embedded, with formation of a new circulation This experiment was followed by successful operation upon both sexes and upon fowls The essayist concludes that the procedure is practicable, that the material can be preserved a reasonable time prior to operation, that the hormone of the implanted gland is helpful in chronic disease, senility, defective sex-development, certain skin conditions, mild arteriosclerosis and anemia, and that it is not necessary that the implanted gland should remain permanently to secure beneficial results The priority of Voronoff, of Paris, in the field is disputed, the author having found no scientific contributions from his pen prior to his visit to this country

—C R

(GONADS) Pseudo-hermaphroditism (Pseudo-ermaprodictismo androgeno) Massari (G), Gazz degli Osp (Milano), 1921, 42, 872

Report of a post-mortem examination The patient gave the impression of a man with normal external sexual organs The scrotum, however, was empty In the abdomen near the inguinal region uterus was found with two bodies, resembling ovaries They were however, testicles with vasa deferentia —J K

On the cytological localisation of a peroxydase, and on its presence in the GONAD cells (Sur les localisations cytologiques d'une peroxydase et sur sa présence dans des cellules sexuelles) Prenant (M) Compt rend Soc de biol (Paris), 1921, 85, 808-810

Histological —T C B

(TESTES) Symptoms of eunuchoid feminilism and tuberculosis (Sindrome di femminilismo eunucoide ed infezione tubercolare) Segà (A), Gazz d Osped (Milano), 1921, 42, 946-950

Description of a man of 24 with tuberculosis of the lungs and with small testicles After ingesting 150 gm of glucose a slight glycosuria resulted At autopsy the testicles were found atrophic, with only a small number of canaliculi The connective tissue was enormously developed There were a very few interstitial cells of polyhedral form —J K

Experimental studies on the GONADS in mammals (*Études expérimentales sur les glandes sexuelles chez les mammifères*) Sand (K), J de physiol et de pathol gén (Par), 1921, 19, 305-322

An abstract of the author's book published in Danish in 1918 Some of the conclusions arrived at are Special importance is to be attached to the interstitial cells of Leydig in the testis, the theca-luteal tissue and corpus luteum in the ovary Transplantation of testis, when successful, causes complete development of sexual characters in the male and hypertrophy of the clitoris in the female Transplantation of the ovary into the male causes hypertrophy of the mammary glands The ovary is able to grow in the interior of the testis, thus producing bisexual characters —Physiol Abst

(GONADS) A case of dystrophic geroderma (Su un caso di geroderma distrofico) Tramontano (V), Gazz internaz di med (Napoli), 1921, abst, Pathologica (Genova), 13, 549

With the accentuated hypoplasia of the gonads the patient presents unusual high stature and typical disposition of fat, while the epiphyseal junctions have been considerably delayed The limbs are unusually long and the secondary sexual characteristics are underdeveloped No genital function, no libido The histological examination of the testis showed an alteration of the seminal tubules, absence of the normal cells, small epithelial cells with scanty protoplasm and resting nucleus The condition, more than hormonal, seems to be due to a fault in development of the spermatogenic function of the testis with disfunction of the thyroid and hypophysis

—G V

(GONADS) Proportions of the body and intersexuality as functions of internal secretion (*Körperproportionen und Intersexualität als Ausdrucksformen der inneren Sekretion*) Weil (A), Deutsche med Wchnschr (Berlin), 1921, 47, 1247-1248

A short note There seems to be a relation between the length of the body, the physical sexual signs and the psychical sexual symptoms —J K

(GONADS) The measures of the body in homosexuals as a sign of a specific constitution (*Die Körpermasse der Homosexuellen als Ausdrucksform ihrer spezifischen Konstitution*) Weil (A), Berl

klin Wchnschr, 1921, 58, 1225, and Deutsche med Wchnschr (Berlin), 1921, 47, 1311

The size of the extremities and the trunk depend upon the endocrine system Hypophysis, thyroid and thymus intensify growth The gonads, however, during puberty, prevent further growth The author finds that in homosexuals, male as well as female, the various anatomical indices were abnormal and believes that this is probably due to the abnormal function of the gonads in homosexuality (It is to be noted that this abnormal function has never been definitely proved)—J K

Further investigations on the humoral action of the nerves of the HEART (Weitere Untersuchungen uber humorale Uebertragbarkeit der Herznervenwirkungen) Loewi (O), Klin Wchnschr (Berlin), 1922, 1, 22-23

If the heart of a toad is filled with a Ringer's solution and the vagus or accelerator nerve is stimulated and if after this the Ringer's solution is brought into a fresh heart it has the same effect on this second heart as if its vagus or accelerator were stimulated Hence some chemical substance is liberated, perhaps a cardiac hormone If the vagus and accelerator are stimulated together generally first a vagus and then an accelerator effect is obtained The content of the heart has just the same action on a fresh heart It is, however, possible by a special way of stimulating both nerves together to get only a vagus effect, but also in these cases the content of the heart first produces in a fresh heart a vagus and then an accelerator effect

—J K

Transitory symptoms of HYPERTHYROIDISM following tracheo-bronchoscopy (Syndromes hyperthyroïdiens transitoires provoqués par la trachéo-bronchosopie) Rist (E) & Weiss (M), Bull et mém soc méd des Hôp d Par, 1921, 45, 1405-1409

Report of two cases as described in the title The disturbances are tentatively attributed to the traumatism of the laryngeal mucosa with consequent irritation of the cervical sympathetic connections —F S H

The morphogenesis of the HYPOPHYSIS in the tailed amphibia Atwell (W J), Anat Record (Phila), 1921, 22, 373-390

The development of the pituitary body is studied in Ambystoma and comparisons of the adult morphology made for Necturus, Spelerpes and Amphiuma It is found that the pars tuberalis, which in the Anura becomes detached at metamorphosis to form two discrete epithelial plaques, remains attached to the anterior lobe in the tailed amphibia, even in adult life—Author's Abst

(HYPOPHYSIS) Atypical adiposo-genital syndrome (Syndrome adiposo-genital atypique) Babonneix & Denoyelle, Bull et mém soc méd des hôp d Par, 1921, 45, 1619-1623

Case report of a man of 50 years with mammary hypertrophy, manifest obesity, large head, short neck, atrophy of the hands, cervical kyphosis, strabismus and nystagmus Psychically he was puerile and cyclothymic The sexual apparatus was mediocre, the testicles small Wassermann negative Urine and cerebro-spinal fluid normal The x-ray showed an enlarged sella turcica —F S H

Cytological observations on the pars buccalis of the HYPOPHYSIS cerebri of man, normal and pathological Bailey (P), J Med Research (Boston), 1921, 42, 349-381

A cytological study of the anterior lobe or pars buccalis of the human pituitary, paying especial attention to the presence and numbers of mitochondria In one case of active acromegaly with an eosinophilic struma the mitochondria were not increased This does not render support to the hypersecretion theory of the origin of acromegaly B also describes a method for differential staining of the eosinophilic and basophilic granules and from his studies concludes that while these two types of granular cells arise from indistinguishable reserve or parent cells they never revert The histological findings in eight cases of adenomatous enlargement of the anterior lobe are given Cells of the basophilic type were absent in all This well known fact is discussed without any suggestion of its possible physiological significance In conclusion it is stated that hyperplasia of the anterior lobe in acromegaly is probably secondary to some underlying biochemical disturbance and while it is widely held that this hypertrophy is indicative of hyperfunction, there is no experimental evidence to support such a conception

—D M

Clinical contribution to the HYPOPHYSEAL theory of DIABETES mellitus (Kasuistischer Beitrag zur hypophysären Theorie des Diabetes mellitus) Bleibtreu (R), München med Wchnschr 1921, 68, 1153-1154

A description of a case of diabetes with an enormous polyuria and a slight glycosuria with acetone or diacetic acid

The excretion of NaCl was not the same as in diabetes insipidus Pituglandol had no effect on diuresis An x-ray of the skull showed the sella turcica and the proc clinoides apparently absent As the Wassermann test was negative the author believes that the diagnosis is tumor of the hypophysis Administration of thyroïdin or oophorin had no effect —J K

(HYPOPHYSIS) On the so-called and the true parahypophysis (Over de zoogenaamde en een ware parahypophyse) Bolk (L),

Nederl Tijdschr v Geneesk (Haarlem), 1921, 65, (II) 1913-1914

The parahypophysis or the pharyngeal hypophysis is a small endocrine organ which in man is situated against the base of the skull near the os basilare Bolk states that it takes its origin from the chorda dorsalis He suggests that the term "retropharyngeal body" would be preferable to parahypophysis The structure is not found in many animals, but is regularly present in man It is held that there is probably a relation between the existence of this body and a complicated course of the chorda dorsalis In structure the retropharyngeal body is complicated In addition to the part which has its origin from the chorda dorsalis, another is found which arises from the epithelium of the pharynx A true parahypophysis, arising from the hypophysis, has been observed by Bolk in the dog only —J K

Concerning malignant HYPOPHYSEAL tumors and hypophyseal cachexia (Zur Kenntnis der bösartigen Hypophysenschwulste und hypophysären Kachexie) Budde (M), Frankfurter Ztschr f Path (Weissb), 1921 25, 16-34

Reports a case of malignant pituitary tumor with metastases in a woman, aged 27 years She was first operated on for a tumor in the left side of the neck, which on account of its relation to the carotid artery, was thought to be a carotid gland tumor Microscopic examination at the time showed it to be a malignant epithelial tumor probably of branchiogenic origin The patient failed rapidly and developed signs of brain tumor involving the basal region Autopsy showed a tumor mass 2 cm in diameter occupying the site of the pituitary gland with nodular extension down over the pons and medulla to the foramen magnum There were also metastases in the lungs as well as a recurrence in the neck Examination of the tumor from the several sites revealed a single type The cells were granular The basophilic and acidophilic cells, so characteristic of the anterior lobe of the pituitary, predominated He points out the rarity of metastases in pituitary tumors and the peculiar clinical interest in that there were no symptoms suggesting primary pituitary disease —D M

PITUITRIN-like substance in cerebrospinal fluid Dixon (W E) & Cow (D), Proc Roy Soc Med (Lond), 1921, 14, Sect Ther & Pharm, 6

Normal cerebrospinal fluid has no pituitrin action, after injection of extracts of intestinal mucosa or ovary it appears after an hour to contain a substance with the properties of pituitrin After injection of pituitary extract, the fluid gave the pituitrin effect im-

mediately Extract of testis, epididymus, liver, pancreas choroid plexus, etc., histamine, pilocarpine, and adrenaline had no effect
—Chem Abst., 15, 3869

Cutaneous alterations in toads after removal of the **HYPOPHYSIS**
(Alterations cutanées chez les crapauds hypophysectomisés)
Giusti (L.) & Houssay (B. A.), Compt rend Soc de biol (Paris),
1921, 85, 597-598

Three to ten days after hypophysectomy the skin takes on a deep bronze to black color, while the ventral surface becomes grayish or brown. Ulcerations appear at points of contact with the ground, and sometimes also on the snout and about the eyes. It is interesting to compare these results with those of others who have demonstrated that early destruction of the hypophysis results in albino larvae that do not metamorphose, and raises a number of questions difficult to solve.—T C B

(**HYPOPHYSIS**) A case of acromegaly (Ein Fall von Akromegalie)
Haevel (A.) Munchen med Wchnschr., 1921, 68, 1336

Demonstration of a woman of 28, who shows typical symptoms of acromegaly and who never has menstruated. The symptoms are much more marked on the right side than on the left. No symptoms of brain pressure. The x-ray does not show a large sella, but its base is not distinct. Thyroid is not palpable, skin is fat, no myxedema. Hair growth and genitals normal.—J K

(**HYPOPHYSIS**) A peculiar process of the diencephalic floor in the fetal calf. Holt (E.), Anat Rec (Phila.), 1921, 22, 201-205

A median ventral downgrowth from the floor of the brain is observed in calf embryos from 40 to 310 mm in length. The structure lies just in front of the hypophysis. The author ascribes no significance, either morphological or endocrine, to it.—W J A

Absence of the pars buccalis of the **HYPOPHYSIS** in a 40 mm pig.
Holt (E.), Anat Rec (Phila.), 1921, 22, 207-215

Description of a 40 mm pig embryo showing complete absence of the pars buccalis of the hypophysis. The neural lobe is well developed. The thyroid, ovaries, and adrenals were normal for this stage of development.—W J A

The Histology of the human **HYPOPHYSIS** in kidney disease
(Ueber das Strukturbild der menschlichen Hypophyse bei Nierenerkrankungen). Hoppli (R.), Frankfurter Ztschr f Path (Wiesb.)
1921, 26, 22-49

The work was suggested by Berberling's report of finding an increase in the basophilic cells of the hypophysis in cases of renal

disease The material from the Pathological Institute at Kiel showed 45 cases with renal disease such as chronic glomerular, arteriosclerotic and parenchymatous nephritis, amyloid disease, tuberculosis and congenital cysts Of these, 30, or 66.7% had an increase in the number of basophilic cells in the hypophysis In 75 control cases only 24, or 32% showed an increase in basophilic cells He confirms Berberling's observations No suggestion is offered of the possible physiological significance of these findings—D M

Action of extracts of HYPOPHYSIS on cerebral polyuria (Action des extraits d'hypophyse sur la polyurie cérébrale) Houssay (B A), & Hug (E), *Compt rend Soc de biol (Paris)*, 1921, 85, 681-683

In dogs it has been shown that the injection of extract of hypophysis is followed by an increased secretion of urine for the first two to four hours following the injection If diuresis has been caused by the ingestion of large quantities of water, the injection of hypophysis prevents the absorption of the water, and the diuresis is sometimes diminished The 24 hour quantity of urine varies due to a general depression of the animal, he eats less and drinks less The authors have observed similar effects in animals suffering from polyuria caused by extirpation of the hypophysis, or by puncture of the optopeduncular region The polyuria was augmented in all cases during the first few hours If the polyuria was very marked, there was little effect on the 24 hours quantity, because the animal continued to urinate and to drink If, however, the polyuria was less marked there was a diminution, due to the fact that the animals did not drink as much as usual—T C B

Secretion of the HYPOPHYSIS and of the PARATHYROID glands (Experimentelle Beiträge zur inneren Sekretion der Hypophysis cerebri und der Glandulae parathyreoideae) Izumi (G), *Mitt a d Hyg-Inst u d Path-Anat Inst (Zürich)*, 1920, 37 p

In order to know the function of the endocrinous glands, especially of the pituitary and parathyroid, the author studied the reciprocal relations between the pituitary and parathyroid, the pituitary and thyroid, the thyroid and parathyroid, and the pituitary and gonads, using 49 cats and 127 rats Some of them were castrated and from the others the thyroids or parathyroids were removed totally or partially by a careful operation After clinical observation during two, five and ten months, they were killed by ether narcosis to study the histology of the above mentioned glands The parathyroidectomized rats and cats showed that the chromophile cells, especially basophils, decline remarkably in number and size in the pars anterior of the pituitary, while the chromophobe cells, especially transition and mother-cells increase in number After the removal of the parathyroid, the pituitary body of the rat in almost every case became smaller, while on the contrary, that of the cat

always enlarged from two to four times the normal size. The source of this enlargement is mainly the proliferation of the cellular element of the pars intermedia. In the thyroidectomized cats the pituitary was always enlarged, due principally to proliferation of the pars anterior, but partially to hypertrophy of the lobulus peduncularis. The source of the former is the extreme proliferation of large granulated basophilic cells, and a few of the eosinophilic cells, while the latter has an increase of the epithelial cells, which accumulate much of the secretion in its acinus. According to the author's experiments, enlargement of pars intermedia cannot be demonstrated in thyroidectomized cats, but only in parathyroidectomized. The pituitary of castrated rats was larger than normal and this is due clearly to the appearance of the "castratcells" in pars anterior. Tinctorial reactions indicate that these cells are derived from the eosinophilic cells of pituitary. At the late period of the experiments an increase of the eosinophilic cells in pars anterior also was noted. Feeding the parathyroidectomized rats with phosphorus-cod-liver-oil and calcium lactate had no favorable influence on the opaque degeneration of the teeth that occurred. Total or partial removal of the thyroid or total castration had no clinical effect upon the course of tetany, which is seen after enucleation of the parathyroids of the rat.—Author's Abst

Cysts of the HYPOPHYSIS Kanavel (A B), with pathological report by Jackson (H), Surg, Gynec & Obst (Chicago), 1918, 26, 61-70

Kanavel reports three cases of typical Frohlich's type of hypophyseal disease. All of these patients were operated upon by a technique described by the author. In each instance there was a cyst in the region of the hypophysis. One of the specimens was carefully studied by Jackson, who found it to be typical of the cysts described by Erdheim as originating from remains of the cranio-pharyngeal duct. These tumors, which are usually cystic, closely resemble adamantinomas. The wall of the cyst here described showed masses of stratified epithelium sharply demarcated from the connective tissue stroma by a layer of tall cylindrical cells resembling the basal cell layer of a mucous membrane. Between this basal layer and the cavity of the cyst there were several strata of flattened cells with intercellular bridges like the prickly cells of the stratum spinosum. Here and there were areas of epithelial cells undergoing hydropic degeneration with the formation of small pseudocysts. No cells of the pituitary body were found in the sections. The article is well illustrated.—J P S

(**HYPOPHYSIS**) Pituitrin in obstetrics (Nog eens mijn standpunt tegenover het gebruik van pituitrine in de verloskunde) Kouwer (B J), Vox medicorum (Utrecht), 1921, 21, 185-186

Warning against careless use of pituitrin without strict indications —J K

(HYPOPHYSIS) A case of dwarfism (Ein Fall von Zwergwuchs)
Maas (O), Berl klin Wchnschr, 1921, 58, 681

The patient was 32 years old and 123 cm tall During the preceding three years he had become very stout He had no hair in the axillae and poorly developed pubic hair, the testicles were normal and the penis large The skiagram showed changes in the sella turcica There was no goiter Intelligence was good Metabolism was low The diagnosis was hypophyseal dwarfism —J K

(HYPOPHYSIS) A simple method of obtaining premature eggs from birds Riddle (O), Science, 1921, ns 54, 664-666

Eggs of various stages of immaturity are obtained without killing the bird, by the injection of 0.22 cc "Pituitrin" in the Ring-dove Injections are best made intramuscularly Eggs are laid, usually from 6½ to 25 minutes following the injection They were laid at stages of immaturity varying from 4 to 26 hours

—F A H

The therapeutic uses of the anterior PITUITARY gland Scott (T B) & Broderick (F W), Practitioner (London), 1921, 107, 278-287

The authors point out that there has been widespread use of the posterior lobe extract, but comparatively little clinical use in England of "Pitglandin," the "active principle" of the anterior lobe The influence of this portion of the pituitary on growth and sexual development is then referred to and attention is called briefly to gigantism and acromegaly, as respectively preadolescent and post-adolescent hyperpituitarism, and to the pre- and post-adolescent deficiency syndromes Anterior lobe therapy is recommended for rudimentary development of uterus and ovaries with scanty menstruation or amenorrhoea, also for enuresis, for some cases of epilepsy, and combined with thyroid for premature senility From the fact that the anterior pituitary influences bone growth, its extract is advised in dental caries and to help calcify the teeth, especially when combined with parathyroid and suprarenal This combination was fed to a rabbit and at the end of two months the incisors of the "plurigland rabbit" were perceptibly longer than those of the control from the same litter These teeth were analysed for the total amount of inorganic matter and the total calcium content The authors give the impression that anterior pituitary extract (oral administration) is beneficial in many conditions, but little proof is submitted —H L

Experimental criticism of the biological dosage of the hypertonic principle of the HYPOPHYSIS (*Critique expérimentale du dosage biologique du principe hypertonisant de l'hypophyse*) Stern (L), & Peyrot (R), *Compt rend Soc de biol (Paris)*, 1921, 85, 804-806

Trendelenburg and Borgmann claim to have determined quantitatively the efficacy of hypophysis extract by comparing its action with that of histamine on the uterine horn of the guinea pig. Their results contradict some observations of the authors and they have gone over the matter again, by establishing the minimum quantity necessary to produce augmentation of tonus in smooth muscle. Their tabulated results show such variations from experiment to experiment, that they conclude there is no constant agreement between the action of histamine and various preparations of hypophysis, and that the content of active principle cannot be determined by this procedure.—T C B

(HYPOPHYSIS) An investigation of some of the factors which may determine the keeping qualities of infundibular extract Tate (G), *Pharm J (Lond)*, 1921, 106, 486-505

The extract, exposed to direct Hg-vapor light for 1 hr at 8-in distance, deteriorated only about 5%, in white or amber glass ampoules it retained its activity. As to the effect of heat and acidity, the results of Adams, Fenger and Hull, and Abel and Nagayama are quoted. Tate found no decrease of activity in a certain extract after boiling for 30 minutes (the extract being "thermostable"), nor upon exposure of the same extract to 38 degrees for 25 days after addition of 0.2 to 2% AcOH in 5 samples. Tate thought a thermostable extract might be serviceable after storing in a tropical climate, e g, in India, but parallel experiments on samples of the same origin and the same acidity did not bear out this assumption. Keeping such drugs at a temperature not above 80 degrees F will probably best prevent excessive deterioration. In discussion, the claim of permanency of these extracts on boiling is doubted. The methods of physiological testing need re-investigation.

—Chem Abst 15, 3895

(HYPOPHYSIS) Experimental gigantism produced by feeding pituitary gland Uhlenhuth (E), *Proc Soc Exper Biol & Med (N Y)*, 1920, 18, 11-14

By feeding anterior lobe of pituitary several *Amblystomae* have been made to grow materially beyond normal size. The experiments were controlled both by keeping certain animals under the same conditions as the pituitary fed and by comparing the "giants" with the largest specimens found in museums. Anterior lobe feeding produced accelerated growth only in the post-larval stage.

Posterior lobe feeding retarded growth The magnitude of overgrowth is indicated in the proportion between the lengths of one experimental and one control animal, namely 264 192 mm

—R G H

Tumor of the HYPOPHYSIS Wechsler (I S), Neurol Bull, N Y, 1918, 1, 331-334

A clinical report of a male white patient, aged 45 years, the major clinical symptoms being blindness, severe constant frontal headaches, without signs of acromegaly or of Fröhlich's syndrome, but x-ray examination showed an enlarged and eroded sella turcica The differential clinical diagnosis was tumor of the pituitary —D M

Psychical disturbances in diseases of HYPOPHYSIS (Psychische Störungen bei hypophysärer Fettsucht) Weygandt (W), München med Wehnschr, 1921, 68, 1356-1357

The following cases are reported

1 A girl who had regular menstruation when she was 15, stopped when she was 16½ When she was 17½ she grew fat and menstruation returned Abderhalden's reaction was positive An x-ray examination showed an enlarged sella turcica She died when she was 22½ At post-mortem a gliosarcoma of the base of the brain was found During her disease she was always extremely bright

2 A boy of 15, was already very fat, at 13 months the x-ray examination was positive Psychically he was an idiot with a very vivid temper The penis was very small, the scrotum did not contain testicles

3 A boy of 19 with dystrophia adiposo-genitalis He is very cheerful, and inclined to caress any person he sees He is restless

4 A boy of 17 with dystrophia adiposo-genitalis Abderhalden's reaction with hypophysis positive He is always cheerful, talks nonsense The administration of pluriglandular extracts resulted in improvement

5 A woman of 32 with adiposity Sella turcica normal Abderhalden's reaction with thyroid positive, with hypophysis negative Her psychical development is that of a child of 5 Her greatest pleasure is to play with a doll (according to the description this was not a case of dystrophia adiposo-genitalis)

From these and other cases it is concluded that in diseases of the hypophysis, whether they are caused by tumor, by hydrocephalus or by another pathological process there exist psychical symptoms Imbecility and idiocy is frequently met with The temperament is generally cheerful with a special inclination to wit and jesting —J K

Cytological notes relative to the **HYPOPHYSIS** (Notes cytologiques relatives a l'hypophyse) Winiwarter (H de), Compt rend Soc de biol (Paris), 1921, 85, 871-874

Histological —T C B

(**HYPOPHYSIS**) Retarded eunuchoidism caused by syphilis (Spat-eunuchoidismus auf syphilitischer Basis) Wittgenstein (A) & Kroner (K), Berl klin Wchnschr, 1921, 58, 1185-1186

A man of 47 was apparently normal till he was 43, then he showed symptoms of weariness and a positive Wassermann test. His aorta was large, as was shown by x-ray examination. He had the look of an old man, a dry skin. Psychically he was depressed, his sexual desires had disappeared. The diagnosis dementia paralytica was made. His voice became gradually high pitched and he was drowsy. His hair was brittle, he was very fat, he had nearly completely lost his beard, his pubic and axillary hair. The penis was small, the testicles atrophic. The sugar tolerance was higher than normal. There was polyuria. The authors believe that the disorder is caused by syphilitic disease of the posterior lobe, although the skiagram of this region was negative —J K

A brief experimental study of the morphology of the heart muscle following **HYPOTHYROIDISM** Brooks (H) & Larkin (J), Am J Med Sci (Phila), 1918, 155, 66-70

Rabbits were thyroidectomized and the hearts removed and examined from 2 days to 6 weeks after the operation. No morphological changes in heart musculature were found —F S H

INFANTILISM and **DWARFISM** (Zur Kenntniss des Infantilismus und Zwergwuchses) Brandis (G), Deutsches Arch f klin Med (Leipz), 1921, 136, 323-346

A careful report of three cases with a good review of the pathogenesis of infantilism. One case of infantilism in a woman of 27, is of interest because of the fact that the sella appeared normal, bone development was retarded, there was no alimentary or adrenalin glycosuria, and treatment with pituitary and ovary gave no results.

—J K

The nature of innervation and its relations to the **INTERNAL SECRETION** (Über das Wesen der Innervation und die Beziehungen zur Inkretbildung) Abderhalden (E), Klin Wchnschr (Berlin), 1922, 1, 7-8

It is not yet known precisely how the nerves act upon the organs which are innervated by them. It is possible that in the stimulated nerve a substance is formed which acts upon the muscle

or on the glands The author gives a review of the newer literature bearing on this subject —J K

The importance of the INTERNAL SECRETIONS in diseases of the skin especially in psoriasis (Die Bedeutung der inneren Sekretion bei Hautkrankheiten, speziell bei Psoriasis) Weinhardt München med Wchnschr, 1921, 68, 1405

The author believes that psoriasis is an endocrine disturbance In a number of cases x-ray treatment of the thymus was followed by cure or at least by a very marked improvement —J K

INTERSTITIAL cells PLACENTA toxin and eclampsia (Ueber interstielle Zellen Placentatoxin und Eklampsie) Fellner (O O), Zentralbl f Gyn (Leipzig), 1921, 45, 1435-1441

The author described a "feminin Sexuallipoid" He found it in corpus luteum, placenta interstitial cells of ovary and testicle This substance contains a toxic material which is volatile, soluble in alcohol, ether and acetone, and probably is an amine of a lipid Subcutaneous injection of this substance in animals produces spasms and in larger doses death It is, however, not probable that it has anything to do with the pathogenesis of eclampsia —J K

Studies on the conditions of activity in endocrine glands VIII
Some effects on the denervated heart of stimulating the nerves of the LIVER Cannon (W B) & Urdil (J E), Am J Physiol (Balt), 1921, 58, 353-364

After removal of the adrenals stimulation of the splanchnic causes a faster rate of the denervated heart Stewart and Rogoff attribute this to rise of pressure, increased mobilization of sugar, etc The authors have investigated this phenomenon, and found that it occurs when the vena cava is closed just below the liver, also when the portal vein is closed If the hepatic artery and portal vein are closed the effect is greatly reduced or abolished Massage of the liver will itself induce a faster heart rate Section of the hepatic nerves shows no increase of the heart beat, or an increase of only 2 beats per minute Stimulation of the hepatic nerves causes more or less increase of heart rate The inference is drawn that some agent arising in the liver is the occasion of the faster beat This can account for the discrepancies in Cannon's and in Stewart and Rogoff's results —T C B

The terminal phenomena after MENOPAUSE induced by x-rays (Die Auffallserscheinungen nach der Rontgenmenopause) Fuchs (H), Strahlentherapie (Berl u Wien), 1921, 12, 742

On the basis of 69 cases the author compares the terminal condition of women in whom an artificial menopause has been pro-

duced according as that condition has followed an x-radiation, ovariectomy, or hysterectomy The paper is entirely clinical and goes into some detail He claims that under x-rays psychical equilibrium is better preserved, vasomotor changes are fewer, and there is less disturbances of the entire generative system—Med Sci 5, 284

MENSTRUATION and OVULATION Frankl (O), Dublin J M Sc, 1921, 4, 481-491

An excellent review of the present status of our knowledge of the subject It embraces a discussion of the relation of various endocrine glands to the genital organs—E N

Experimental study of the physiology of MENSTRUATION (Contribución experimental para el estudio de la fisiología de la menstruación) Ramirez (E), Rev Mex de Biol (Mexico), 1921 2, 24-33

Menstruation is intimately connected with the function of the ovaries No corpora lutea are found at the beginning of either menstruation or rutting, hence they are not the determining cause of menstruation On the other hand, the chondrioma of the small interstitial cells of the ovary in animals in rut are formed with enormous activity Lipoid substances are also produced During rutting the modifications of the uterus are wholly comparable to those during menstruation The secretion of the interstitial tissue produces the catemenial symptoms and is probably eliminated in the flow, which contains a great quantity of lipoids distinct from cholesterin When the uterus is lacking and the ovaries persist, true phenomena of intoxication and vicarious hemorrhages appear Histologic study of the uterus during menstruation and cytological study of the menstrual detritus from the cervical canal show that a substance of ovarian origin produces uterine cytolysis The ovarian hormones may be clearly demonstrated by the Abderhalden reaction, allowing the sanguineous serum to act on the uterine mucosa, except during menstruation the reaction is negative Uterine mucosa can advantageously be used as substrate in the Abderhalden pregnancy test—Author's abst (abbreviated)

Influence of MENSTRUATION on the food tolerance in DIABETES mellitus Rosenbloom (J), J Am M Ass (Chicago), 1921, 76, 1742

This paper contains studies on 2 cases of diabetes mellitus in which the patients lost all their food tolerance with the onset of their menstrual period Two tables are presented, showing that when the patients were put on starvation diets, the glycosuria that previously developed during menstruation did not reappear One of the patients later, during her menstrual period, developed an acute

acidosis and died During this period she was on a diet that had previously kept her sugar-free and free from acidosis The author believes that the explanation of the loss of food tolerance in the 2 cases described is some temporary alteration in the function of the gonads, either an increased secretion or a lack of correlation with other of the endocrine organs —E N

A study of the hemoglobin after childbirth with special reference to the resumption of MENSTRUATION Rucker (M P), Am J Obst & Gyn (St Louis), 1921 1, 964-972

From a study of 74 cases, Rucker reaches the conclusion that hemoglobin is a deciding factor in the post-partum resumption of menstruation Immediately after delivery there is a definite drop in the hemoglobin, from which the patient slowly recovers The average parturient begins menstruating when the hemoglobin reaches about 75 per cent Certain subjects menstruate with a much lower hemoglobin, and there are patients who have had some anemia for a long time Retrodisplacement with its pelvic hyperemia is also a factor in the early restoration of the menstrual phenomenon

—E N

Diseased condition of bones and joints as influenced by MENSTRUATION Rugh (J T), Penn M J (Harrisburg), 1921, 25, 261-264

Three interesting cases are recorded in which the bone and joint symptoms were considerably aggravated during each menstrual period In one patient with a tubercular hip, the sinus resulting from aspiration of tuberculous pus which had been closed for 2 months, burst open during a menstrual period and discharged blood for several days, this stopped with cessation of the menstrual flow In another patient operation for villous arthritis of the knee happened to be performed the day after menstruation ceased, and a peculiar brownish synovial membrane was encountered and ten ounces of blood serum escaped from the joint—vicarious menstruation Schuman in discussing Rugh's paper protests against operating at the menstrual period except in emergencies —H L

Mental deficiency or MONGOLISM Ward (A C), Med J Australia (Sydney), 1921, 11 326

A case report Patient was being treated with thyroid —R G H

(OVARY) The use of Bohnstedt's migraine serum in gynecology [Die Verwendbarkeit des Migraneserums (Bohnstedt) in der Gynakologie] Abel (G), Deutsch med Wchnschr (Berlin), 1921, 47, 1229-1230

There seems to be a relation between attacks of migraine in women and the ovaries French authors have even described a

"migraine ovarienne" Bohnstedt has prepared a serum from placenta (the manner of preparation is not given) He found that an intramuscular injection of this serum diminishes the activity of the ovaries and has a good influence on migraine Abel reports good results with the use of this serum in three women It is said to give good results also in men (There is not a trace of real pharmacological or chemical study in the whole article The manner of preparation of the serum is not given The article has a decidedly commercial aspect)—J K

The nerves in the human OVARY with particular reference to their termination (Über die Nerven, insbesondere deren Endigungen, in menschlichen Eierstöcke) Akagi (Y), Frankfurter Ztschr f Path (Weissb), 1921, 26, 165-187

The literature dealing with anatomical studies of nerve distribution to the ovaries is summarized as follows They enter at the hilus with the blood vessels, there are ganglion cells in the hilus and also in the substance of the ovary, most of the ovarian nerves are vasomotor, the Graafian follicles are supplied with nerves but whether they enter the membrane granulosa is doubtful, nerve endings are numerous in corpora lutea and also in the interstitial cells In these studies the silver impregnation methods of Ramon y Cajal and Bielschowsky were used The ovaries of 11 human cases ranging from infancy to middle life and including cases with true and false corpora lutea were studied It is concluded that the muscle fibers, the vessels, capillaries and especially the stroma cells are supplied with nerves The interstitial or stroma cells are particularly rich in nerve endings Nerve endings were found particularly abundant in the hyperplastic theca interna of atresic follicles and also in the theca interna of ordinary follicles The terminal nerve fibres may appear as points or as bulbs—the former being more frequent Contrary to other observers very few nerve endings were found in the superficial layer of the true and never in the false corpus luteum —D M

A new proof of the internal secretion of the OVARY (Ein neuer Beweis für die innere Sekretion des Ovariums) Asher, Deutsche med Wchnschr (Berlin), 1921, 47, 1480

Hyperglycemia caused by administration of diuretin disappears after removal of the ovaries Parabiosis with a normal female restores the diuretin-hyperglycemia Extirpation of the testicle has no influence —J K

(OVARY) Experimental studies following oophorectomy Bailey (H C), Am J Obst & Gyn (St Louis), 1921, 2, 77-83

A review of the literature The principal deductions are that experimental work is inconclusive as regards the demonstration of

a direct effect of an ovarian secretion on the energy metabolism of the cell, that no ovarian change may be demonstrated following hysterectomy until after three or four months, that the menopause ensues even though the ovaries remain, if the uterus is entirely removed, and that symptoms are prevented by saving a portion of the uterine mucous membrane, so that menstruation may occur, and that transplantation of the ovary is of no value in relieving menopausal symptoms, unless the uterus, or part of it, remains

—E N

OVARIAN sterilization at one exposure by the help of the x-rays
(La stérilisation ovarienne en une seule séance à l'aide des rayons de Rontgen) Bécère (A), J de radiol et d'électrol (Paris), 1921, 5, 67

This critical review of Bécère traces the development of the x-ray treatment of fibromyomata from its inception by Foveau de Courmelles in 1904 to the present methods by the late Professor Kronig, and continued by Seitz and Wintz. The chief part of the review is devoted to an examination of the efficacy and desirability of the German method, which consists in giving at one séance a dose of radiation which is calculated to the desired results. From a careful examination of the publications which have issued from the Fribourg and Erlangen clinics, Bécère finds a not unimportant difference in the dose which is administered at the two institutions, for what must be considered the same object. Kronig and Friedrich estimate what they call the "ovarialdosis" to be 20 per cent of the "erythemdosis," whereas the "Kastrationdosis" of Seitz and Wintz is 34 per cent of the same quantity. This difference may possibly be referable to an inequality of the standard employed at the two centres, namely, the erythema dose. The main questions raised by Bécère are two. First, can the changes in the ovary be brought about by a single application of x-rays with certainty? From an examination of published results he states that this cannot be done, and that it may therefore be necessary to repeat the exposure. The second question centers round the desirability of such single exposure methods. The economical advantage is, in his opinion, counterbalanced by the ill effects upon the patients which frequently supervene upon these prolonged exposures to x-rays, and which are not often met in the conservative method of spacing the irradiations over a considerable length of time. Bécère also discusses in some detail the arguments which have centered round the question as to whether the diminution in size of a fibroma is a sequel to the changes initiated in the ovary or whether it is due to a direct action of the rays upon the growth. The argument is well considered and the paper is a valuable one. It contains a useful bibliography, in which we fail to find the name of a single British author.—Med Sci

Action of OVARIAN products on the cutaneous reactions of tuberculin (*Action de produits ovariens sur les cuti-réactions a la tuberculine*) Bouveyron (A), *Compt rend Soc de biol (Paris)*, 1921, 85, 836-837

While the cutaneous reaction to tuberculin in young tubercular females is intensified during menstruation, various ovarian products such as the liquid from the follicles, concentrated glycerine extracts of corpus luteum, or the whole ovary, or the ovary deprived of its follicles and corpora lutea, completely suppresses, or attenuates the reaction. A congestive halo appears in about ten minutes, and lasts several hours, but disappears before the tuberculin reaction.

—T C B

Nature of luteinic and interstitial cells of the OVARY (*Sulla natura della cellula luteinica e della cellula interstiziale dell ovaio*) Brugnattelli, *Boll d soc med chir di Pavia, (Milano)*, 1919, —, —, *Abst Pathologica (Genova)*, 1921, 13, 25

The author made tissue cultures from the ovaries of rabbits. He obtained no growth with ovaries in a state of rest, and hardly any result from the ovaries at the end of pregnancy. Strikingly positive results were obtained from ovaries during the breeding period and at the beginning of pregnancy. The development proceeds rapidly until the tenth day, when degeneration begins to appear. The author states that the luteinic cell and the interstitial cell are not of epithelial origin, but connective, and both elements are of the same nature. He infers that these cells can be classified among the great category of adventitial cells. The hypothesis is strengthened by the periodical appearance of imposing masses of luteinic and interstitial cells in the ovary during the breeding period and the pregnancy. (See also *Endocrin*, 5, 806) —G V

(OVARY) Discontinuity in the morphological evolution of the chondriome of the egg of Sabellaria alveolata L (*Discontinuité dans l'évolution morphologique du chondriome de l'oeuf de Sabellaria alveolata L*) Fauré-Fremiet (E), *Compt rend Soc de biol (Paris)*, 1921, 85, 986-989

Histological—T C B

Transplantation of OVARY Fleischmann (K), *Wiener klin Wchnschr*, 1921, 34, 621

Data will be reported elsewhere —J K

The OVARY after hysterectomy for fibroids (A follow-up study) Hawks (E M), *Am J Obst & Gyn (St Louis)*, 1921, 1, 959-963

The paper is based on a series of 84 cases in which a follow-up study was made. The onset of flushes was delayed when one ovary

was left and further delayed when both were left The severity was diminished when one ovary was left and almost eliminated when both were left Only one case had both pain and swelling in an ovary In all the 65 cases in which one or both ovaries had been left, there were 12 subjects, or one in five, who had any trouble with the retained ovary In 11 of the 12 it was temporary The conclusion drawn is that it is better to leave healthy ovaries after hysterectomy for fibroids done before or near the time of the ménopause

—E N

Effect of undernourishment on mammalian OVARY and the sexual cycle Loeb (L), J Am M Ass (Chicago), 1921, 77, 1646-1648

Loeb reviews his investigations on this and related topics, some of which have been published in biological journals, not always accessible to medical readers Complete excision of the corpora lutea leads to a notable acceleration of ovulation, though not of the process of follicular maturation If the corpora lutea were burnt out instead of excised, ovulation was not accelerated, as the burning caused an injury of the remaining ovarian tissue and particularly of the follicles Young follicles remained alive and even began to develop, but their vitality was much diminished, and they usually become atretic before reaching medium size Such ovaries, characterized by the presence of only small and small-to-medium sized follicles, at a period of the sexual cycle at which there should have been present large ones, he designates as hypotypical ovaries In these ovulation can not of course take place Loeb has found that such a hypotypical condition of the ovaries may occur spontaneously in certain guinea pigs A considerable number of experiments have shown also that unfavorable nutritional conditions, due either to outside factors or to a pathologic state within the animals, may be responsible for a similar condition of the ovaries Experimental studies have shown that the follicles retrogress because the degeneration of isolated granulosa cells sets in at an early stage, and this degeneration is so pronounced that the loss of cells far exceeds their new formation The underfeeding affects primarily the epithelial elements (the granulosa), to a minor degree the connective tissue is also affected Recent studies by Walsh have shown that the ovum is responsible for the growth of the follicles and, ultimately, of the whole ovary It is clear that a hypotypical condition of the ovaries is incompatible with ovulation and the normal course of the sexual cycle The uterus in such cases usually is found to be thin and inactive—E N

(OVARY) Further investigations on the origin of tumors in mice

VI INTERNAL SECRETION as a factor in the origin of tumors
Loeb (L), J Med Research (Boston), 1919, 40, 477-496

The experiments here reported were carried out upon mice in which had been previously followed the normal cancer rate and the cancer age through a number of generations, and in which the cancer rate and cancer age had been found to be approximately constant. Loeb concluded that "a hormone given off by the ovary regulates those tissue changes which lead to the development of cancer of the breast in mice." The influence is a quantitatively graded one. For, castration practiced at the age of 3 or 4 months completely or almost completely prevents the appearance of carcinoma of the breast in mice. In mice castrated at the age of 5 to 7 months, cancer appears, but "in all probability the tumor rate is lowered and furthermore the tumors appear later in life." In mice castrated above the age of 7 months, the frequency with which tumors appear is not markedly affected, but "possibly the age at which the tumors appear is somewhat higher." These observations suggest that the tissue changes which eventuate in the development of cancer, occur at a very early period in life, and that castration affects these primary tissue changes rather than the secondary transformation of these changes into fully developed carcinomatous growth. Prevention of breeding in mice lowers the tumor rate and raises the tumor age slightly, but its effect is not comparable to that of an early castration. Transplantation of the ovaries of the sisters into young castrated male mice belonging to strains with a high tumor rate did not lead to the development of tumors in the male mice. This Loeb interpreted as indicating that the transplanted ovaries did not function with the same completeness and in the same rhythm as normal ovaries in the female mice. The effect of hormones on the development of cancer is a specific one. A hormone influences the development of cancer only in those organs to which under normal conditions it has a specific relation. Three factors are active in the development of cancer: (a) heredity, (b) irritation (physical stimulation), (c) internal secretion (chemical stimulation). Wherein the heredity factor consists is not certain at present. Internal secretion seems to cause cancer only in co-operation with hereditary factors. On the other hand, hereditary factors need—at least in the case of certain cancers—the co-operation of hormones in a definite quantity, if cancer shall develop.—J P S

The chemical composition of the OVARIES of fresh water gar, *Lepidosteus* Nelson (E E) & Greene (C W), J Biol Chem (Balt), 1921, 49, 47-56

A report of the analysis of 12 samples of gar ovaries in which figures for lipoid, protein, water and extractive solids, ash, total nitrogen, amino nitrogen and creatine are given.—F S H

Function of the OVARY during menstruation and in metrorrhagia
(Intorno alla funzione dell' ovario nella mestruazione e nelle me-

trorrhagie) Perazzi (P), *Folia gynaec (Pavia)*, vol XII, n 1, abst, *Pathologica (Genova)*, 1921, 13, 25

Previous researches proved the existence of specific ferments for determined proteins as shown by the Abderhalden reaction Perazzi obtained a strongly positive reaction with ovary substrate and the serum of women suffering with so-called idiopathic metrorrhagia Hence he postulates a relation between metrorrhagia and altered function of the ovary The same phenomenon is found to a certain extent during menstruation —G V

On the evolution of the adult OVARY of the rabbit (*Sur l'évolution de l'ovaire adulte de la lapine*) Salazar (A L), *Compt rend Soc de biol (Paris)*, 1921, 85, 783-784

Of histological interest —T C B

A case of OVARIAN tumor in a mulatto Stone (I S), *Washington M Ann*, 1918, 17, 253

Not of endocrine interest —E N

OVULATION and MENSTRUATION as post-operative considerations Watkins (T J), *Am J Obst & Gyn (St Louis)*, 1921 2, 489-493

Ovulation and menstruation as post-operative considerations are important because many of the pelvic operations affect these functions The usual good health which obtains after the menopause demonstrates the ability of the endocrine glands to compensate for the loss of ovarian secretion The author believes that the difference in severity between the neuroses of the natural and the artificial menopause is negligible He advocates the conservation of the ovaries whenever possible in cases of uterine fibroids and salpingitis Conservation of menstruation has no value aside from its relation to reproduction The function should be abolished by excision of the body of the uterus in the course of abdominal pelvic operations when conditions obtain which make pregnancy impossible or inadvisable —E N

Researches on the function of the PANCREAS (*Untersuchungen über die Funktion des Pankreas*) Adler (L), *Arch f exper Path u Pharmakol (Leipzig)*, 1921, 91, 110-124

The temperature-raising and awakening effects of thyroid extract upon the hibernating hedge-hog is lessened or entirely destroyed if the animal is treated with pancreas extract from another hibernating animal A similar retarding influence is exerted upon thymus extract or adrenin by administration of pancreas extract

—W J A

(PANCREAS) Un médicament usuel l'opothérapie pancréatique Faroy (G), Prog méd (Paris), 1921, 36, 361-362

A review in which it is concluded that so far as internal secretion is concerned, pancreas preparations are useless except, perhaps, in certain cases of "hyperhepatic diabetes"—R G H

The essential atrophy of the PANCREAS Oertel (H), J Med Research (Boston), 1919, 40, 289-294

Under this title Oertel describes a lesion of the pancreas in which "quantitative loss and collapse of parenchyma are the only essential elements and occur independently of either vascular or inflammatory changes or an increase in fibrous connective tissue" The writer has observed five cases All of these patients had a severe, even acute, diabetes, ending in coma and death—J P S

Toxic necrosis and regeneration of the acinar cells of the PANCREAS Parker (F, Jr), J Med Research (Boston), 1919, 40, 471-476

"Toxins which cause lesions of the heart, liver, kidney and adrenal, cause similar lesions in the acinar cells of the pancreas, which have heretofore been overlooked The acinar cells of the pancreas have great powers of regeneration" Arsenic was found to cause necrosis of the pancreas as well as of the liver, kidney and adrenal—J P S

Action of PANCREATIC extract injected into the blood of a diabetic animal (Action de l'extrait pancréatique injecté dans le sang, chez un animal diabétique) Paulesco, Compt rend Soc de biol (Paris), 1921, 85, 555-557

The chief symptoms of total extirpation of the pancreas are an augmentation of the proportion of sugar in the blood and urine, an augmentation of the proportion of urea in the blood and urine, an augmentation of the acetone bodies in the blood and urine The intravenous injection of pancreatic extract causes a diminution or even a transient suppression of the hyperglycemia and glycosuria, a diminution or transient suppression of the urea in the blood and in the urine, a notable diminution in the acetonemia and acetonuria Tables of experimental results are given—T C B

Influence of lapse of time after the intravenous injection of PANCREATIC extract in a diabetic animal (Influence du laps de temps écoulé depuis l'injection intraveineuse de l'extrait pancréatique chez un animal diabétique) Paulesco, Compt rend Soc de biol (Paris), 1921, 85, 558

The effect of pancreatic extract on the glycemia and glycosuria commences immediately after the injection, attains a maximum in about 2 hours, and lasts about 12 hours—T C B

Influence of the quantity of PANCREAS employed in preparing the extract for injection into the blood of a diabetic animal (Influence de la quantité de pancréas employée pour préparer l'extrait injecté dans le sang chez un animal diabétique) Paulesco, *Compt rend Soc de biol (Paris)*, 1921, 85, 558-559

The effect of the extract varies with the quantity of gland employed—T C B

Action of PANCREATIC extract injected into the blood of a normal animal (Action de l'extrait pancréatique dans le sang chez un animal normal) Paulesco, *Compt rend Soc de biol (Paris)*, 1921, 85, 559

Pancreatic extract injected into the jugular of a normal dog, caused a diminution in the blood sugar, as well as in the urea of the blood and urine—T C B

Xanthomatosis in a case of recurrent PANCREATITIS (Ueber Xanthomatose in cinem Fälle rezidivieren der Pankreatitis) Wynhausen (O J), *Berl klin Wehnschr*, 1921, 58, 1268-1270

An interesting case A very fat man, who was intemperate in eating and drinking and who had cases of diabetes in his family twice received a severe trauma on the abdomen First he developed a general xanthomatosis, this receded and recurred from time to time During such an attack the cholesterol content of the serum was enormously increased The xanthomata disappeared when the patient took only a little fat and reappeared when he took much fat At the same time he had attacks of glucosuria and of a disturbed external function of the pancreas (undigested muscle fibres but no fat in the stools) It is probable that the pancreas has a certain relation to the cholesterol metabolism—J K

The comparative effects of PARATHYROID and THYROID feeding on growth and organ hypertrophy in the white rat. Cameron, (A T) & Carmichael (J), *Am J Physiol (Balt)*, 1921, 58, 1-6

At the present time there is a tendency to consider the actions of thyroid and parathyroid as opposite in nature Thyroid feeding inhibits growth in young white rats, and causes hypertrophy of various organs The present study has to do with the effect of parathyroid feeding on growth and hypertrophy of the organs The experiments were carried on with the usual technique Six rats developed tetany The results show that even very heavy doses of parathyroid produce no definite effect on growth, and no organ-hypertrophy—T C B

A discussion of the PARATHYROID question with particular emphasis on the acidophilic cell (*Beitrag zur Epithelkörperchenfrage, unter besonderer Berücksichtigung der Acidophile der Zelle*) Koopman (H), *Frankfurter Ztschr f Path* (Weiss), 1921, 25, 342-372

The author has studied the morphological appearance of the parathyroids in 261 cases, including six cases of paralysis agitans. He confirms work of the most recent observers that there are no characteristic pathological changes in the parathyroids of paralysis agitans. He reviews briefly the commoner alterations found in the parathyroid as hemorrhage in infancy, hypertrophy and hyperplasia in rickets and osteomalacia, adenoma, and then goes into a discussion of the occurrence of the acidophilic cells of the gland. As is well known, these acidophilic cells may occur singly and in groups scattered irregularly through the gland. In the 255 cases grouped according to age, he found the frequency of acidophilic tissue to increase with age. Thus, of 36 cases in the first decade of life, none showed acidophilic cells, of 12 cases in the second decade there were 2, of 30 cases in the third decade there were 12, of 41 cases in the fourth decade there were 16, of 34 cases in the fifth there were 18, of 23 cases in the sixth, 16, of 40 cases in the seventh, 23, of 27 cases in the eighth, 23, and of 12 cases in the ninth decade of life there were 9 cases with acidophilic cells. He thus confirms the generally accepted opinion that the acidophilic cells in the human parathyroid are rarely seen before puberty, then the frequency progressively increases with each decade. He points out that Erdheim, using morphologic methods had found these acidophilic cells poorer in lipoids than the basophilic types and his observations bear this out. He thinks the acidophilic cells may be considered the morphologic expression of the internal secretory activity of the gland.—D M

The treatment of tetania PARATHYREOPRIVA (*Über die Behandlung der Tetania parathyreopriva*) Eiselsberg (A), *Wiener klin Wchnschr*, 1922, 35, 1-2, München *med Wchnschr*, 1921, 68, 1540

In 20 years the author carried out 2588 strumectomies with 6 fatal cases of tetany. The treatment of this form of tetany consists in administration of parathyroid tablets (3-4 daily), calcium lactate up to 30 grams daily, afeinil intravenous during the attacks, clysters with chloral and a diet without flour. Only in cases in which this treatment proves unavailing should grafting be tried.—J K

(PARATHYROID) Muscle tonus II The point of attack of guanidine and methylguanidine in the production of motor irritability. Guanidine-cocaine antagonism. Frank (E) & Stern (R), *Arch f exper Path u Pharm* (Leipzig), 1921, 90, 168-179

An antagonism between guanidine and cocaine (or novocaine) was demonstrated in the frog. Experiments on the response to electrical stimuli after guanidine intoxication indicate that guanidine acts upon the "receptive substance" of the sarcoplasm and not upon the muscle substance in general. Synthetically prepared methylguanidine acts qualitatively exactly as guanidine.

—Chem Abst

(PARATHYROID) Paralysis agitans Jakob, Berl klin Wchnschr, 1921, 58, 1393-1394

Demonstration of a patient with Parkinson's disease, markedly improved by suggestion. This is cited as disproving the significance of the case of endocrine "cure" of Parkinson's disease reported by Köhl. (See abstract in this issue) —J K.

(PARATHYROID) Paralysis agitans Köhl, Berl klin Wchnschr, 1921, 58, 1393

Demonstration of a patient with Parkinson's disease, markedly improved after implantation of a parathyroid —J K

Hyperplasia of the PARATHYROID in human rickets Pappenheimer (A M) & Minor (J), J Med Research (Boston), 1921, 42, 391-403

A careful histologic study was made upon parathyroid glands from 14 children with rickets and 18 non-rachitic children. Glands of children of corresponding ages were compared. There was found a very definite increase in the size of these glands in children with rickets. This increase in size was due to actual multiplication of the cells and not to an increase in size of the individual cells. The parathyroids of children within the first 18 months of life consist almost entirely of "plant-like cells with very clear unstained cytoplasm, round large nuclei, and clear cell outlines." In rickets there was no constant nor characteristic change in the cell type, and the clear cell remained markedly predominant. In this series of cases there was no increase in the supporting tissue of the parathyroids in rickets and no increase in the vascular supply or congestion of the blood vessels not found equally in non-rachitic patients. The state of nutrition of the child had no bearing on the size either of the gland as a whole or of its individual elements —J P S

PARATHYROID gland changes in rickets and other diseases of bone (Über Epithelkörperchenbefunde bei Rachitis und anderen Knochenerkrankungen) Ritter (C), Frankfurter Ztschr f Path (Weiss) 1920, 24, 137-176

This paper reviews the morphologic changes found in the parathyroids in cases of rickets, osteogenesis imperfecta, osteomalacia,

and Moeller-Barlow's disease, coming to post-mortem examination in the Pathologic Institute at Freiburg In rickets the parathyroids are often slightly enlarged, hyperemic, edematous and occasionally showing increase in the stroma The enlargement is less common in early cases than in long standing severe rickets In Moeller-Barlow's disease (one case) the parathyroids were normal In osteomalacia and osteoporosis, the parathyroids were never found atrophic but often enlarged In one case of osteomalacia the clear vegetable-like cells predominated, but in all the others the darker, more basophilic type predominated, just as in the cases of long standing and severe rickets In general his observations confirm those of Erdheim

—D M

(PARATHYROID) Experiment in new method of therapy of paralysis agitans Weinberg (M H) & Schubb (T), Soc Exper Biol & Med (N Y), 1921, 19, 21

Starting out from the premises that paralysis agitans is due to hyperparathyroidemia, as advocated by several observers, we proceeded to prepare a parathyroidectin substance for the treatment of this condition Experiments were conducted on rabbits and on goats The two external parathyroid glands of the goat were removed, and after forty days the blood of the goat was withdrawn and glycerinized The administration of this blood to Parkinsonian patients seems to show promising results Further study of this method of therapy is now under way—Quoted

PERSPIRATION in man (Beobachtungen uber die Schweisssekretion beim Menschen) Pelier (S) & Strisower (R), Wiener Arch f inn Med, 1922, 3, 297-308

Many patients with diabetes perspire very little or not at all Aspirin or pilocarpin do not cause perspiring When adrenalin or thyroidin are given with aspirin or pilocarpin in diabetes perspiring occurs This is not due to suggestion, as the combination of aspirin or pilocarpin with a solution of NaCl is inactive Perspiring is independent of the amount of water in the body Patients with hypothyroidism also show a raised perspiration after the administration of thyroidine It is highly probable that the perspiring is regulated by endocrine processes via the autonomic nervous system

—J K

The functional effects of the PINEAL gland and its tumors (Die Zirbel und ihre Tumoren in ihrem funktionellen Einfluss) Askanazy (M), Frankfurter Ztschr f Path (Wiesb), 1920, 24, 58-77

This paper discusses the morphology of pineal gland tumors, the function of the pineal gland and points out the possible cor-

relations of the pineal gland particularly with the sex glands Teratomas and cysts are the most common forms of "tumors" The literature reports show that many of these cases have shown precocious sexual development and in support of this clinical observation some of the experimental work is reviewed, especially that with fowls in which removal of the pineal gland resulted in enlarged sex glands —D M

Primary tumors of the PINEAL gland (Über primäre Tumoren der Zirbeldrüse) Giebel (W), Frankfurter Ztschr f Path (Weissb), 1921, 25, 176-190

Reports the clinical and autopsy findings of two patients with tumors of the pineal gland In one of these was a sarcoma in a male, aged 25 years This tumor was of indefinite morphology and on account of the lymphocytic and eosinophilic infiltration and polymorphic type of the tumor cell a more specific classification could not be suggested In fact, it was due to its staining characteristics with Van Gieson's and Mallory's connective tissue stains that it was grouped as a sarcoma The second was a walnut-sized dermoid cyst in a boy aged 15 years This patient clinically had vague symptoms of brain tumor, unlocalizable The literature is reviewed and, including the above two cases, there are reported 53 primary tumors grouped as follows Sarcomas, 13, teratomas, 10, cysts, 7, hyperplasias, 7, gliomas, 5, psammomas, 3, carcinomas, 3, angiomas, 1, undetermined nature, 4 —D M

The action of PLACENTAL and TESTICULAR lipoids on the male and female sex-organs (Ueber die Wirkung des Placentar- und Hodenlipoids auf die männlichen und weiblichen Sexualorgane) Fellner (Otfried O), Arch f d ges Physiol (Berlin), 1921, 189, 199-214

Injection of placental and ovarian lipoids produces a diminution of testes, especially shrinking of canals In ripe rabbit testes spermatogenesis ceases, and the sperm cells degenerate Detritus-type masses form in the lumina Degeneration also takes place in unripe cells Interstitial tissue increases Signs of epithelial degeneration are seen in the epididymus Testicular lipoids produce similar effects The action is not specific since other lipoids produce it Testes of new-born children show similar appearances, similarly to be referred to placental lipoids of the mother Seminal vesicles and prostate do not appear to be affected macroscopically Testicular lipoids show the same physiological properties when injected into females as do ovarian and placental lipoids, enlarged uterus with numerous deep glands, and enlarged mammae This growth-producing action is specific It is considered probable that the active chemical substance in these lipoids is identical The

author reviews the evidence in an endeavor to ascertain which cells produce these lipoids —A T C

Internal secretion of PLACENTA (*Ueber die innere Sekretion der Plazenta*) Puppel (E), *Deutsche med Wchnschr* (Berlin), 1921, 47, 1294-1295

The author prepared what he called a placenta-opton, made by allowing the placenta to undergo sterile autolysis. The preparation appears to be of value in obstetrics because of its effect in stimulating uterine contraction. It has no galactagogue effect. In one case of sterility it was injected, with successful results, in a second, it failed. Good results were obtained in two cases of dysmenorrhea

—J K

(PLACENTA) Experiments on animals with placenta-opton (*Tierversuche mit Plazenta-Opton*) Kratzeisen, *Deutsche med Wchnschr* (Berlin), 1921, 47, 1260

Five cc of 5% solution of placenta-opton was injected subcutaneously every two days into young guinea pigs and albino rats. When 30 cc had been given the animals were killed. The mammae were found to be larger than in the controls and the uterus and vagina were nearly always double the normal size. The wall of the uterus showed hypertrophy of the muscle fibers, the epithelium also was thicker and the number of glands increased. Similar experiments reported by other authors have generally been accompanied by a hemorrhagic nephritis. This Kratzeisen could not confirm. It must be borne in mind that other experimenters have employed ether and alcohol extracts —J K

Experimental studies on the toxicity of PLACENTAL lipoids in their relation to the etiology of puerperal eclampsia (*Experimentelle Untersuchungen uber die Toxizität von Placentalipoiden, mit Bezug auf die Aetio-genese de Puerperal-eklampsie*) Schonfeld (H E H), *Arch f Gynäk* (Berlin), 1921, 115, 80-125

A characteristic review of the literature. Personal experiments of S yield the conclusions that the alcohol, acetone and glycerin extracts of the placenta contain constrictor toxins which are thermolabile and insoluble in ether. They act electively on liver cells, but are also toxic for kidney cells, and vascular endothellum. The nucleus is primarily affected. There was observed a constrictor, a thrombosis producing, a partuition facilitating and a liver, kidney and endothelial poison in the extracts. The relation between these toxins and eclampsia is stressed —F S H

Retarded RICKETS and starvation osteopathy (*Spatrachitis und Hungerosteopathie*) Simon (W V), *Veröffentlichungen aus dem Gebiete der Medizinalverwaltung* (Berlin), 1921, 14, 351-443

The osteopathy seen during and after the war is not a new disease, but belongs in the group of rickets and osteomalacia. This form of "Kriegs-osteopathie" is due to a pluriglandular insufficiency. The author considers the skin as an endocrine structure and especially as a chromaffin organ. Thus perhaps may be explained the fact that these diseases are seen especially in places and houses where there is not enough light. This explains also perhaps the splendid effect of the treatment of rickets with artificial sunlight. The causes of the "Hungerosteopathies" are (1) Defective feeding, (2) Intoxication, (3) Influences on the skin (want of light, dirt, etc.). The best treatment is phosphorus-cod liver oil, calcium, adrenalin, strontium lactate, fresh air, light and massage.—J. K.

Treatment of SCLERODERMIA with x-rays (Zur Röntgenbehandlung der Sklerodermie) Donath (J.), München med. Wchnschr., 1921, 68, 1326-1327

The author believes that the thyroid plays an important part in this disease. It is specially a hypofunction of this gland. In two cases he observed improvement by giving thyroid X-rays when they have a good effect must stimulate the thyroid and not as Hammer in a previous paper stated decrease its function.—J. K.

SECRETIN V Its effect in anemia, with a note on the supposed similarity between secretin and vitamin B Downs (A. W.) & Eddy (N. B.), Am. J. Physiol. (Balt.), 1921, 58, 296-300

Fully grown rabbits were fed on a diet consisting exclusively of polished rice until the blood count fell to four million. They were then put on a full diet of oats, turnips, carrots and cabbage. One group of six rabbits received in addition a subcutaneous injection of 20 mgm. per kilo body weight of dried secretin in saline solution. A second group of four controls received like injections of saline solution only. All the animals improved in weight and blood count, but the secretin animals showed an increase of 27.3 per cent over the normal blood count at the end of the eighth week, while the controls had barely reached the normal. The secretin group showed an average increase of 145 gms. above the original weight, while the controls were 108 gms. below the original. Could this marked improvement be brought about by an equivalent excess of water soluble vitamin? Five rabbits were injected with secretin. Within an hour the blood count had increased 17.55 per cent, and the second count was still higher. Five other rabbits were injected with equivalent amounts of vitamin from brewer's yeast. The blood count remained about the same as before injection. The number of red cells in circulation was not increased.—T. C. B.

Anatomical modification of the SPLEEN following THYROIDECTOMY (Le modificazioni anatomiche della milza consecutive a

tiroidectomia) Baggio (Gino), Arch di Fisiol (Florence), 1921, 19, 89-100

Rabbit spleens show a considerable reduction of weight (absolute and relative) following thyroidectomy. The atrophy of the organ is not accompanied by any particular alteration of structure. It is directly related to the course and origin of the general cachexia or the organism, and its extent is parallel to the former —A T C

Anatomical modifications of the SPLEEN following stimulation (Le modificazioni anatomiche della milza consecutive a stimolazione) Baggio (G), Arch di Fisiol (Florence), 1921, 19, 299-315

Spleens of rabbits stimulated daily for periods varying from 20 to 80 days showed in 78 per cent of the cases a diminution of weight averaging 0.182 gm, usually accompanied by a diminution of body weight. Thyroidectomy produces similar results (Baggio, Arch di Fisiol, 19, 89). No definite histological changes were detected. The number of lymphocytes was diminished —A T C

SPLENIC syndromes Mayo (W J), Surg Clin N Am (Phila.), 1921, 1, 1307-1325

A survey of five syndromes illustrating the fact that pathologic conditions found in the spleen are obviously closely related to the pathology of the blood. Reports of cases of splenic anemia, hemolytic icterus, pernicious anemia, polycythemia, and splenomyelogenous leukemia, in all of which splenectomy was performed are detailed. The author reminds us that the spleen, while concerned with the purification of the blood, with the filtration from the blood of worn-out red blood cells and infectious and toxic material, and their direction to the liver, is not the principal but rather an agent. Twelve out of 270 splenectomized patients could be put into no known classification. The author concludes that it is best at this time to regard the spleen as little known territory, through which a few trails have been blazed —C R

The correction of STERILITY Maier (F H), The Penn M J (Harrisburg), 1921, 25, 78-82

After discussing the several anatomic abnormalities, infectious and other pathological causes of sterility, mention is made of the endocrinopathic origin. The latter may be of ovarian nature, or due to pre- or post-adolescent thyroid or pituitary insufficiency. Usually obesity and amenorrhoea accompany the sterility in females. When the correct origin is determined the appropriate gland extract, thyroid, pituitary or corpus luteum may occasionally cure the sterility. The outlook is better if one can recognize the mild forms of endocrine deficiency when organotherapy is more promising. In discuss-

ing the above paper, Jump and Anspach agree in the main with the author's remarks, but sound a note of caution in expecting too much from ductless gland extracts at the present time—H L

Certain dietary factors in the causation of STERILITY in rats
Reynolds (E) & Macomber (D), Am J Obst & Gyn (St Louis), 1921, 2, 379-394

Careful studies by means of deficiency diets of one type or another led the authors to the following conclusions A moderate decrease in the percentage of the fat soluble vitamine, of the protein, or of the calcium contained in an otherwise excellent diet produces a definite decrease in the fertility of individual rats A slight decrease in the fertility of both partners will produce a sterile mating The fertility of the mating may be stated as the product of the fertility of the individuals concerned If the index so obtained falls below a given point the mating will be sterile, and this result holds true whether the partners are of equal or of widely different fertility These principles explain the fact that two individuals which are sterile when mated together may nevertheless reproduce freely if mated to new partners (of higher fertility) Dietary deficiencies produce a lowered fertility which varies in degree with different individuals, though of the same parentage and in the same cage Diminished fertility sometimes results in the appearance of abortion More percentage deficiency in both proteins and calcium produces visible ill health and great infertility—E N

(TESTES) Conditions determining the secondary SEX characters in the Urodela (Sur le conditionnement des caractères sexuels secondaires chez les Batraciens Urodèles) Aron (M), Compt rend Soc de biol (Paris), 1921, 85, 482-484

Histological discussion of the paratesticular tissue as the homologue of the interstitial tissue in mammals—T C B

(TESTES) On the structure of the wall of the seminiferous tubules (Sur la structure de la paroi propre des canalicules séminipares) Bologna (V) & Goldner (J), Compt rend Soc de biol (Paris), 1921, 85, 586-588

Histological—T C B

Presence of TESTIS and uterus in the hernial sac of a man (Presenza di utero e testicolo nel sacco erniario di un uomo) Bolognesi (G), Arch f klin Chir (Berlin), May, 1921, Abst, Pathologica (Genova), 13, 549

In the hernial sac of a left inguinal hernia of a male otherwise offering a normal development of all the other external sexual characteristics, an undescended testis has been found and an infantile uterus with tube The testis offered the characteristics of

cryptorchidism The uterus and tube were rather developed The author points to the noteworthy persistence of embryonal duplicity Only one sexual gland had been found, but the local operation does not exclude the presence of ovary in the patient The most interesting feature of the case is the relatively good development of uterus and tube—G V

(TESTES, PROSTATE) Is rejuvenation after prostatectomy a Steinach effect (Ist die Verjungung nach der Prostatektomie als Steinacheflekt aufzufassen)? Blum (V), Wiener klin Wchnschr, 1922, 35, 2-4 ^c

It is often observed that after prostatectomy the patient appears younger Is this caused in the same way as Steinach's rejuvenation? Steinach and his pupils state that prostatectomy is followed by an obliteration of the ducti ejaculatorii This, however, is not only not true, but when after a prostatectomy the ducti ejaculatorii are obliterated this must be considered as due to a serious breach of technic by the surgeon If Steinach were right the hypertrophy of the prostate, which compresses the ducti ejaculatorii, ought to give rejuvenation The term "hypertrophy" of the prostate as generally used is incorrect It is much better to call it an adenoma of the prostate It is remarkable that this adenoma contains a substance, which, when injected into dogs, causes intoxication and death In normal prostates this substance is not found In the same way in the blood of patients with prostatic hypertrophy eosinophilia is found This disappears after the operation It is, therefore, much more probable that the rejuvenation after removal of the adenoma is due, not to an obliteration of the ducti ejaculatorii, but to the removal of a tumor having a toxic influence on the organism—J K

(TESTES) On the conditions determining the secondary SEX characters in fishes (Sur le conditionnement de caractères sexuels secondaires chez les Poissons) Courrier (R), Compt rend Soc de biol (Paris), 1921, 85, 486-488

Is there in the fishes an interstitial gland as in mammals, and if so does it influence the secondary sex characters? The stickleback was chosen for a solution of this question because it has at the time of reproduction well marked secondary characters Its ventral surface becomes a scarlet red, and the kidneys are transformed, the nephrocytes are charged with large secretory granulations which furnish an abundance of mucus An histological study of the testicle before and during reproduction shows a testicular interstitial gland, but it differs from mammals in being limited to a certain period of the year—T C B

On the existence of an interstitial gland in the TESTICLE of fishes (Sur l'existence d'une glande interstitielle dans le testicule des

poissons) Courrier (R), Compt rend Soc de biol (Paris), 1921, 85, 939-941

Chiefly histological, showing the existence of interstitial glands in the testicles of a number of species of fish—T C B

Vitamine studies VII The influence of fresh alfalfa upon the weight of TESTES in single-comb white leghorn cockerels Dutcher (R A) & Wilkins (D D), Am J Physiol (Balt), 1921, 57, 437-443

Not of endocrine interest—T C B

Sarcomatous abdominal TESTICLE in a hermaphrodite Halpenny (J) & Kinneard (G), Canad M Ass J (Montreal), 1921, 11, 632

The writers cite Swale Vincent and Bouin and Ancel to prove that the essential for a hermaphrodite is not spermatozoa and ova, but the presence of the internal secretion of both testicle and ovary. The article reports a case clinically described as a hermaphrodite. The diagnosis of a large abdominal tumor lay between a fibroid uterus and a sarcomatous testicle. At operation it was proven to be the latter, by a specimen removed for section. No ovary was found. It is suggested that an abdominal testis is more liable to malignancy than is the scrotal organ. Therefore, if it cannot be placed in the scrotum by operation, its ablation is indicated. It is doubted if any surgical transplantation of testis or ovary can be so successfully carried out that a hermaphrodite can be converted into a creature having distinctive sex characteristics.

—Author's Abst (J H)

(TESTES) Criticism of rejuvenescence according to Stemach (Critique du rajeunissement selon Steinach) Hanak (A), Compt rend Soc de biol (Paris), 1921, 85, 698-699

If the development of the attributes of virility, and the sexual character in the male is regulated by the testicles, we must ask if it is possible to restore these attributes and the sexual instinct in an individual with senile atrophy of the testicles. If the testes produce an excitant for the anaplastic phase of development, whence comes the excitant for the cataplastic phase? The problem of rejuvenescence is strictly linked to that of senescence—T C B

Changes in transplanted TESTES (Ueber das Schicksal frei transplantierten Hoden) Kleeberg, München med Wchnschr, 1921, 68, 1133

The experiments were made in guinea pigs. The cells of the seminal epithelium become necrotic. Twenty days after transplantation the whole organ is generally necrotic and granulation

tissue has begun to grow from the periphery to the center The invading cells look like macrophages and contain much fat Cholesterol is not present The interstitial cells do not increase in number or volume, but become necrotic like the seminal cells The author does not believe that the transplanted glands assume any special endocrine function—J K

(TESTES) On the retardation of masculinisation after partial castration (*Sur le ralentissement de la masculinisation dans la castration partielle*) Lipschütz (A), Ottow (B) & Wagner (Ch), *Compt rend Soc de biol (Paris)*, 1921, 85, 630-632

After partial castration, a retardation of development of the sex characters has been occasionally observed One could think of this as due to a diminished internal secretion, but such a theory is not in accordance with observed fact Guinea pigs also show this, but examination proves that the remaining fragment of testicle has degenerated, cicatrized or even disappeared This was not the case in the rabbits The remaining fragment was in a state of development corresponding to the age of the animal at the time of operation As the mass of testicle left in situ (one-quarter to one-half of one testicle, the other being entirely removed) was sufficient for normal masculinisation, we must explain the sexual infantilism as due to the infantilism of the remaining testicular fragment *Eunuchoidism* is caused either by infantilism or retrograde development or complete destruction of the respective tissues of the testicle

—T C B

The prostate and roentgen exposure of the TESTICLES Neménow (M), *Ztschr f Urol (Berlin & Leipzig)*, 1921, 15, 45-49

Neménow experimented on dogs and found that the prostate became enlarged after exposure of the testicles to the roentgen rays The seminiferous cells in the testicle atrophied while the Leydig cells proliferated, and he theorizes that the latter—as the producers of the internal secretion of the testicle—secrete more profusely as they proliferate and this excessive secretion entails the hypertrophy of the prostate This is analogous to clinical experience As spermatogenesis dies out in elderly men, the Leydig cells proliferate and the prostate hypertrophies secondarily, as in the experiments on dogs, the microscopic changes in the testicles being identical He is now making microscopic examination of the testicles and prostate in elderly cadavers to see whether they sustain his view It warns, he adds, of the need of caution in accepting Steinach's operation which, unfortunately, he continues, was published too early

—J Am M Ass, 78, 157

Spontaneous disappearance of certain secondary SEX characters in a cock Histological study of the TESTICLE (*Disparition spon-*

tanée de certains caractères sexuels secondaires chez un coq
Étude histologique du testicule) Portier (P) & de Rorthays
 (Mlle R), *Compt rend Soc de biol (Paris)*, 1921, 85, 444-446

A cock hatched in June, 1919, developed normally as regards sexual instinct and secondary sex characters. One year later, in June, 1920, there began a rapid modification. He became "triste," ceased to crow, isolated himself in one corner of the barnyard, and was indifferent to the presence of the female. He died in August, and the testes were found to measure only 12 mm, the size of the normal at two months. Their weight was 0.6 gm, where the normal varies between 14 and 40 gms. The histology of the testicles is given, showing a return to the embryonic condition. These facts confirm those obtained experimentally by ablation of the testicles. Attention is called to the fact that the total weight of the testicles is near the inferior limit which Pezard estimated to be essential for development of the secondary sex characters.—T C B

Senile changes of the TESTIS and prostate in dogs Smith (L W),
J Med Research (Boston), 1919, 40, 31-50

Simple senile atrophy of the testicle from vascular sclerosis is entirely lacking as a pathological entity. Testicular atrophy is accompanied by epithelial, mesothelial and endothelial changes. These may be degenerative or proliferative. The epithelial changes, when degenerative, begin centrally in the tubules, when proliferative they begin usually with the basal cell layer of spermatogones. The mesothelial changes are usually proliferative and show an increase of either the interstitial cells or the connective tissue stroma or both. The endothelial changes, when degenerative, are sclerotic and are indicative of atrophy, when proliferative they are usually an accompaniment of tumor formation. Senile testicular tumors are apparently of two general types: those derived from the epithelium of the tubules, and those derived from the interstitial cells. The cells of these tumors all show a tendency toward the undifferentiated prepubertal type of cell development, with the power of mitosis in growth, but not in differentiation and specialization. Epithelial changes are localized primarily in single tubules. Several adjoining tubules may become involved by extension or fusion with a resultant single tumor nodule or with an apparently focal area of atrophy. The usual epithelial atrophy is a mucoid degeneration of the cytoplasmic elements, beginning centrally in the tubules. The interstitial cell in senility undergoes a characteristic diminution in size with an accumulation of large brownish pigment granules and the gradual obliteration of its lipid content.—J P S

Modern views on the transplantation of TESTICLES (Der gegenwärtige Stand der Hodenüberpflanzung) Stabel, *Deutsche med Wchnschr (Berlin)*, 1921, 47, 1248

In six cases of homosexuality the author has transplanted a testicle, but has never seen any good result from it —J K

(TESTES) The experiments of Regnier de Graaf and the functions of the seminal vesicles (*L'expérience de Régnier de Graaf et les fonctions des vésicules séminales*) Wertheimer (E), & DeBois (Ch), *Compt rend Soc de biol (Paris)*, 1921, 85, 504-505

Not of endocrine interest —T C B

Clinical and pathological aspects of TETANY (*Beitrag zur Klinik und Pathologie der Tetanie*) Elias (H) & Spiegel (E A), *Wiener Arch f inn Med*, 1921, 2, 447-460

In human tetany the inorganic phosphorus content of the serum is increased The phosphorus of the lipoids does not change In serious cases the inorganic phosphorus content is often higher than in slight cases There are, however, exceptions The increased amount of phosphorus is certainly not due to the contractions or spasms of the muscles The hyperphosphoremia seems to be an important symptom of tetany —J K

A case of spindle cell sarcoma of the THYMUS with discussion of the occurrence and importance of glandular elements in the thymus (*Ein Fall von Spindelzellensarkom der Thymus, zugleich ein Beitrag zur Frage und Bedeutung des Vorkommens drüsiger Elements in der Thymus*) Brand (O), *Frankfurter Ztschr f Path (Weissb)*, 1920, 24, 445-465

This paper reports the case of a male, aged 28, dead of cerebro spinal syphilis in which a mediastinal mass had been recognized during life and a clinical diagnosis of gumma of the pericardium made The post-mortem examination showed an encapsulated tumor mass 9x7x3 cm in the lower pole of the thymus area Microscopic examination showed it to be a spindle cell sarcoma rich in blood vessels—a kind of angiosarcoma There were numerous elongated branching glandular spaces lined with cuboidal and columnar epithelium Outside the tumor mass definite thymic tissue with formed Hassall's corpuscles were present These glandular spaces are probably the remnants of the embryological ducts of Remak from whose involution many believe the Hassall's corpuscles are formed It is suggested that the tumor arose from a portion of the fetal thymus which during development failed to differentiate into normal thymic tissue —D M

Various appearances of the hepatic cell in the tadpoles of *Rana temporaria* fed with THYROID (*Divers aspects de la cellule hépatique chez les têtards de Rana temporaria nourris avec de*

la thyroïdes) Dragonu (J) & Fauré-Fremiet, Compt rend Soc de biol (Paris), 1921, 85, 434-436

Histological—T C B

The phenomena of caryorrhexis in the human THYMUS (Les phénomènes de caryorrhexis dans le thymus humain) Dustin (A P), Compt rend Soc de biol (Paris), 1921, 85, 1103-1105

Histological—T C B

(THYMUS, THYROID) Modification of germplasm by hormones (Versuche uber Keimesanderung durch Inkreteinflusz) Grote (L R), Deutsche med Wchnschr (Berlin), 1921, 47, 1461-1462

The author gave to male and female mice thymus opton or iodothylin He observed that the offspring of father, mother or both that had been treated with thymus opton showed a retarded growth, though they were born with a normal weight The young of animals to which iodothylin was given grew in some cases more rapidly than the control animals, in another case the growth was normal—J K

The question of the small THYMUS cortex cell (Zur Frage der kleinen Thymusrindenzellen) Pinner (M), Frankfurt Ztschr f Path (Weissb), 1920, 23, 479-498

Discusses the old question of the origin and nature of the small lymphocytic cell of the thymus Are they of endodermal or of mesoblastic origin? Concludes with the majority of recent authors that these cells may be identified with true blood lymphocytes

—D M

On the THYMUS (Over de thymusklier) Lebeer (J), Vlaamsche geneesk Tijdschr (Gent), 1921, 2, 400-410

An excellent review The author points out that it has never been proved that the thymus is an endocrine organ He considers it probable that it has something to do with the regulation of nuclein metabolism—J K

Gland physiology XLVII The relation between THYMUS, spleen and bone-marrow (Beitrage zur Physiologie der Drusen XLVII Mitt Leon Asher Die Beziehung zwischen Thymus, Milz und Knochenmark) Matsuno (G), Blochem Ztschr (Berlin), 1921, 123, 27-50

Rabbits of nearly the same age and size were used in these experiments No particular diet was fed The animals were bled, splenectomized or thymectomized, or combinations of the operations were done and the effect of these procedures on the bone-marrow studied by hemoglobin, erythrocyte and leucocyte counts on the

blood The effect of the administration of HCN on control and test animals was also determined Extensive protocols and charts are given The conclusion is made that the thymus exerts a stimulating influence on bone-marrow The removal of the spleen does not alter the picture produced by thymectomy—F S H

(THYMUS) Concerning status thymo-lymphaticus (Tets over den status thymolymphaticus) Meursing (F), Geneesk Bl Klin en Lab v d prakt (Haarlem), 1921, 22, 347-380

A very good general review of the literature The author found a remarkable number of large thymi in people who had come to accidental deaths He denies that there is any relation between status thymicus and a narrow aorta—J K

Exposure of the hyperplastic THYMUS to x-rays in myasthenia pseudoparalytica (Über die Röntgenbehandlung der hyperplastischen Thymus bei Myasthenia pseudoparalytica) Pierchalla (L), Therap Halbmonatsh (Berlin), 1921, 35, 504-505

A woman of 48 with a typical myasthenia pseudoparalytica, with a normal thyroid, but a large thymus-shadow was treated by x-rays The symptoms disappeared as did the myasthenic muscle reaction This cannot be called a definite cure, however, there may be a remission Nevertheless the patient has now for many months been able to do her work—J K

THYROIDECTOMY under local anesthesia Allen (C W), Am J Surg, Q Suppl Anesth (N Y), 1921, 35, 12-13

A brief description of the author's technique for infiltration anesthesia in thyroidectomy, which he prefers in every case, regional anesthesia offers little advantage It is pointed out that in removing the thyroid under local anesthesia it is preferable first to divide the isthmus to avoid the unpleasant choking sensation and increase the mobility of the two lobes—C R

(THYROID) X-ray treatment of toxic goiter Allison (R G), Beard (A H) & McKinley (G A), Am J Roentgenol (N Y), 1921, 8, 635-640

In an exhaustive study of the x-ray treatment of toxic goiter the authors have given the following data and conclusions Of the 27 cases of Graves' disease without complications, who were subjected to x-ray treatment, but were not operated upon, 24 are well, both from the clinical and laboratory standpoint The treatment has been complete for nearly eight months The remaining 3 cases came to operation Of these three, one, they feel, was definitely improved before operation, the other two were normal a few months after operation Of 6 cases of post-operative hyperthyroidism, which had relapsed, one showed a definite cure The other 5 showed no

improvement Of three cases of thyrotoxic adenoma none showed any responses to x-ray therapy The only subject of the series who was operated upon during an increasing basal metabolic rate died an operative death The results obtained in the earlier cases might have been attained more quickly if more intensive therapy had been used No bad results or complications, which could be attributed to the treatment occurred in any of the series Their experience with this treatment was convincing that only with the closest possible co-operation between the clinician and the roentgen therapist, can satisfactory results be obtained—P L C

Ten years of serum treatment for HYPERTHYROIDISM Beebe (S P), Interstate M J (St Louis), 1918, 25, 161-171

During the last ten years Beebe has treated some 4,000 cases of hyperthyroidism with antithyroid serum, the results being summarized in the present article The author first answers certain theoretical and clinical criticisms which have been offered from time to time by various investigators The results from, and the method of employing, antithyroid serum are quite different from the use of antidiphtheritic and antitetanic sera in the respective diseases Antithyroid serum is the only therapeutic serum employed which is derived from injection of a human antigen Its employment, therefore, requires great caution and must extend over a long period of time Other therapeutic measures, such as rest, proper diet, etc, must accompany the use of the serum—J P S

THYROID disease and the war Beebe (S P), Med Rec (N Y), 1918, 93, 237-238

The author anticipated a considerable increase in hyperthyroidism both among the soldiers and the civilians, as a result of the emotional crisis produced in action and by the nature of war Fright, sudden danger such as soldiers encounter and profound grief and worry such as wives, mothers and sisters experience, naturally produce many instances of pathological thyroid activity Beebe especially urges that proper provision for suitable treatment of such soldiers be made, pointing out that the general army hospital is not conducive to improvement or cure—H L

Ten cases of THYROID disease Beebe (S P), Med Rec (N Y), 1918, 93, 705-711

This is a report of nine cases of varying degrees of hyperthyroidism and of one case of carcinoma of the thyroid The treatment of each patient is given in some detail—J P S

Malignant neoplasm of the THYROID with metastases in the intestine and bone Binnie (J F), Surg, Gynec & Obst (Chicago), 1918, 26, 288-291

This is a report of a case of spindle cell sarcoma believed to have been primary in the thyroid gland. There were no clinical symptoms indicating interference with the function of this gland. The feature of greatest interest, because of the rarity with which it is encountered, was the metastasis in the intestine. Only two cases showing similar secondary tumors were found in 40 cases of sarcoma of the thyroid collected from the literature.—J P S

Irrregularity of neutralization consecutive to ablation of the THYROIDES and PARATHYROIDES (*Déréglementation neutralisatrice consécutive à l'ablation des glandes thyroïdes et parathyroïdes*) Bisgaard (A), Hendriksen (V) & Larsen (E J), *Compt, rend Soc de biol (Paris)*, 1921, 85, 607-609

Observations on two cases of tetania strumipriva and on a dog with total extirpation of the thyroids and parathyroids, support the theory that hypofunction of the parathyroids is an etiological factor in conditions of spasmophilia, notably tetany and idiopathic tetany. The conclusion is arrived at from a study of the N elimination.

—T C B

(THYROID) The anesthesia problem in goiter surgery from the surgeon's standpoint. Blair (V P), *Am J Surg, Q Suppl Anesth (N Y)*, 1921, 35, 5-6

The author prefers local anesthesia upon patients showing marked hyperthyroidism with intoxication or degeneration in essential organs, in other cases he regards general ether anesthesia preferable to nitrous oxide.—C R

(THYROID) Notes sur le traitement chirurgical des goitres en Suisse. Block (J C) & Charrier (J), *Presse méd*, 1921, 29, 853-854

Technical notes on Swiss methods of goiter surgery.—R G H

(THYROID) Notes on the etiology of goiter (*Note sur l'étiologie du goitre*). Boitel (W), *Rev méd de la Suisse Rom (Genève)*, 1920, 40, 717-746

Boitel comes to the conclusion that the distribution of goiter among the recruits in Switzerland does not agree with the zone described by Hunziker, namely, that corresponding to the climate in the regions between 600 and 1,000 meters, middle height (Abst from Hunziker, *Schweiz med Wchnschr*, 51, 337).—C P McC

The effect of THYROID feeding on growth and organ-hypertrophy, in adult white rats. Cameron (A T) & Sedziak (F A), *Am J Physiol (Balt)*, 1921, 58, 7-13

Thyroid was fed to adult white rats and the results showed a distinct retardation of growth. There was an actual gain in weight

of the liver, kidneys, heart, spleen, lymph glands and adrenals The thyroids averaged a smaller weight These results are in agreement with those found for young animals —T C B

The relation of the **THYROID** gland to the phenomena of immunity (Contribution a l'étude de l'action de la glande thyroïde sur les phénomènes d'immunité) Clevers (J), *Compt rend Soc de biol* (Paris), 1921, 85, 659-661

The rôle of the thyroid in the processes of immunity has not been definitely established Garibaldi thinks extirpation of the thyroid favors the production of hemolysin Others find ablation of the gland has no effect The author has tried to determine experimentally the effect of thyroidectomy on the production of antiovalbumin precipitin He concludes that ablation of the thyroid favors the production of antibodies to ovalbumin —T C B

(**THYROID**) Experimental studies in a case of congenital myxedema (Experimentelle Untersuchungen an einem kongenitalen Myxödem) Cori (G), *Wien klin Wchnschr* (Vienna), 1921, 34, 485-486 *München med Wchnschr*, 1921, 69, 1434

Cori reviews the studies of Mansfield and Pap (*Endocrinology*, 1921, 5, 520) on the heat-regulatory mechanism of thyroidectomized animals The author then reports similar studies on a myxedematous child, 4 years of age The temperature curves were studied, following immersion in a bath at 25° C and in another at 40° C, both before and after thyroid feeding Comparison of the temperature curves shows that in the untreated child the temperature fell to 33° C in the cold bath and did not return to normal for 14 hours Normal children showed an initial fall to 36° C and the normal was regained after 1½ hours After thyroid feeding the behavior of the myxedematous child was that of the normal In the warm bath the myxedematous child did not react There was no reddening of the skin, no sweating and no acceleration of the pulse or respiration Following the parenteral injection of milk the child developed a typical protein fever with a temperature elevation to 39° C, that did not subside for 41 hours The administration of thyroid increased the response of the child to adrenalin and atropin slightly, while it diminished the response to pilocarpin The electrocardiogram described by Zondek as characteristic of myxedema (*Endocrinology*, 1921, 5, 369) was also present in this case —J K

Effect of the ingestion of **THYROID** on the male generative gland (Action de l'ingestion de corps thyroïde sur la glande germinative male) Courrier (R), *Compt rend Soc de biol* (Paris), 1921, 85, 484-486

Observation and experimentation demonstrate that the thyroid hormone produces a trophic excitation of the genital glands Cer-

tain authors, however, do not agree to this Monteroso, for instance, claims that thyroid feeding causes degeneration of the seminal epithelium His animals lost weight, and fasting we know causes genital atrophy This was the problem White rats were used, and care was taken to compensate for the increased metabolism by an abundant alimentation, sufficient to maintain a positive balance Thyroid was fed in addition A rat treated in this way for twenty-one days, during which time he took 75 grams of thyroid and increased in weight 30 grams, had perfectly normal testicles when examined histologically Evidently when we avoid the effects of malnutrition, the thyroid does not cause degeneration of the testicle Neither does the thyroid influence the maturation of the testicle, but after thyroidectomy the thyroid appears to exercise a trophic excitation of the testicle —T C B

Flagellated THYROID cells in the dogfish (*Mustelus canis*) Cowdry (E V), Anat Record (Phila), 1921, 22, 289-299

Flagellae are demonstrated by various methods in the thyroid gland of the dogfish They are present without apparent adaptive value, but may have some bearing upon the problem of the ancestry of the gland, indicating perhaps its development from a flagellated epithelium like the endostyle of ascidians The author holds that the presence of flagella shows that the primary direction of secretion is toward the follicular lumen, and not toward the peripheral blood vessels —W J A

(THYROID) Exophthalmic goiter in a girl of sixteen with special reference to etiology, and end results following ligation without thyroidectomy Crance (A M), Am J Surg (N Y), 1921, 35, 9-12

The etiology in the case reported was believed to be focal infections in teeth and tonsils Improvement was marked after eradication of foci and ligations, but thyroidectomy was not permitted and the patient died, evidently from cardiorenal complications —C R

Certain post-operative complications of operation on the THYROID gland Crile (G W), Lower (W E), Sloan (H G) & Harrison (B T), Am J Surg (N Y), 1921, 35, 317-319

Mention is made of possible attachment of scar-line to trachea; unevenness of neck contour, hoarseness resulting from trauma to nerves, temporary psychic aphonia, and other possible complications The authors administer iodine in simple goiter for a year following operation to prevent rebuilding of the gland, and thyroid extract intermittently where thyroid deficiency is a complication —C R

(THYROID) The anesthesia problem in goiter surgery Crotti (A), Am J Surg, Q Suppl Anesth (N Y), 1921, 35, 2-4

A summary of the comparative merits of general and local anesthesia in thyroid surgery. The author prefers ether in most cases, but emphasizes the fact that hard and fast rules are impossible—that in goiter surgery the important secret of success is to know how to proportion the surgical act to the patient's condition. Failures from an injudicious operation should not be charged to anesthesia.—C R

THYROIDECTOMY—a brief review of 137 cases De Courcy (J L),
Am J Surg (N Y), 1920, 34, 282-285

Observations are made from a series of 137 thyroidectomies with a very low mortality rate. It was noted that the most immediate and permanent results were obtained when both lobes and the isthmus were removed, it being suggested that single lobectomy and ligations are dangerous without being efficient in many cases. The fact is stressed that removal of foci of infection are but preliminary to removal of the diseased thyroid, the eradication of foci not being curative per se.—C R

(THYROID) Treatment of endemic goiter (*Essai de traitement du goître endémique*) Degrafs (P), Progrès méd (Paris), 1921, 36, 524-525

Degrafs believes that, on the whole, best results are to be obtained in endemic goiter by treatment primarily tonic. He relies upon sodium arsenate, strychnia, sodium glycerophosphate and quinine. This treatment, however, is not efficacious in adolescent goiter. He believes that drinking water does not play a major role in the etiology of endemic goiter, but that climatic conditions in general must be considered. Abrupt variations in meteorological conditions are regarded as of especial importance.—R G H

Reactions of the liver cell of frog tadpoles to THYROID feeding
(*Divers aspects de la cellule hépatique chez les têtards de Rana temporaria nourris avec de la thyroïde*) Dragoiu (J) & Fauré-Fremiet (E), Compt rend Soc de biol (Paris), 1921, 85, 434-436

The feeding of thyroid to tadpoles of *Rana temporaria*, after administration of thymus, or of thymus plus starch, produces definite changes in the nucleus and cytoplasm of the liver cells. In the nuclei minute vacuoles appear concerning the nature of which the author hesitates to make any suggestion. In the cytoplasm there is a marked development of so-called parasomes, which the author believes to be identical with similar structures described by Laguesse, Pacaut and Vigier in other cells. Each parasome consists of a central granule which is highly refractive and does not stain easily, surrounded by concentric lamellae. Sometimes they are double. A

single parasome may be larger even than the nucleus The author remarks upon their absence in the pancreas and refrains from any statement of the functional significance of the parasomes —E V C

Histological study of the phenomena induced in the tadpoles of *Rana temporaria* by THYROID feeding (*Étude histologique des phénomènes provoqués chez le têtard de *Rana temporaria* par l'alimentation thyroïdienne*) Draglou (J) & Fauré-Fremiet (E), *Compt rend Soc de biol (Paris)*, 1921, 85, 437-439

A histological study of the accelerated metamorphosis induced by thyroid feeding —T C B

On the existence of evidence of direct continuity between PARATHYROID, THYROID, and THYMUS nodules in mammalia (*Sur l'existence de rapports de continuité directe entre parathyroïdes, thyroïde et nodules thymiques chez les mammifères*) Dustin (A P) & Gérard (P), *Compt rend Soc de biol (Paris)*, 1921, 85, 876-877

Histological —T C B

Anomalies of THYROID function as related to gestation (*Des anomalies de la fonction thyroïdienne dans leurs rapports avec la gestation*) Fruhinsholz (A) & Parisot (J), *Gynéc et Obst (Paris)*, 1921, 4, 169-206

An extensive and well written review of the subject The provisional conclusions of the study are as follows Gestation seems to determine a state of physiological compensatory hyperthyroidism which is more marked in the second period of pregnancy This hyperactivity may become pathological and may manifest itself at different stages of pregnancy Sometimes it does not appear until delivery, just as if it had been maintained in a state of neutralization by the condition of pregnancy Hyperthyroidism is probably not favorable to fecundation When that condition is present before gestation, there often results a diminution of activity, although in exceptional cases an exacerbation may occur Hypothyroidism is more favorable to fecundation When gestation is in progress the hypothyroid condition may be improved if the status is mild, if low, it may be aggravated There is certainly a relation between tetany and pregnancy, and between tetany and parathyroid insufficiency Certain offspring of mothers having thyroid disturbances have a predisposition to glandular troubles which are not necessarily homologous to those of the mother —F S H

The production of heat in tadpoles fed THYROID or THYMUS (*La produzione di calore nei girini alimentati con tiroide o con timo*) Gayda (T), *Arch di Fisiol (Florence)*, 1921, 19, 267-285

Tadpoles of *Bufo vulgaris*, fed with thyroid and showing the phenomena of acceleration of metamorphosis and arrest of growth, exhibit a heat-production which, referred to unit body-weight, is distinctly greater than that of tadpoles of the same age and under the same temperature conditions (15°C), but fed with flesh. The fact is more evident when the tadpoles are kept at a somewhat higher temperature (22.5°C), under the precise conditions which produce greatest thyroid effect on metamorphosis. When, with protracted feeding, the tadpoles tend to remain immobile and cease feeding, the production of heat diminishes progressively yet remains greater than with the flesh-fed tadpoles. *Bufo* tadpoles fed thymus, and exhibiting slight acceleration of growth and retardation of metamorphosis, show a heat production but little greater than that of controls fed flesh.—A T C

(THYROID) A new method for the determination of the fibrin percentage in blood and plasma. Gram (H C), J Biol Chem (Balt), 1921, 49, 279-295

The percentage of fibrin in both plasma and whole blood was found to be higher in one case of Graves' disease than in normal.—F S H

(THYROID) Skin rashes in exophthalmic goiter. Gundrum (F F), Cal State J Med (San Francisco), 1921, 19, 339

The author reviews the literature on skin rashes associated with exophthalmic goiter and notes that the majority of authors have merely described the rashes without undertaking to connect them with physiological effects of hyperthyroidism. Hyde and McEwen in the Amer J Med Science, June, 1903, attempted a classification into three groups, first, dermatoses of accidental concurrence, second, more or less distantly related to the essential morbid processes of goiter, and third, intimately related to the pathology of goiter. A large majority of patients having skin rashes and exophthalmic goiter have belonged within the first or second group. Indeed, it is likely that most of the skin troubles are no more than the results of hypersusceptibility to injury of the moist, congested and often slightly edematous skin. Gundrum reports two cases in which a definite dependence of the rash upon thyroid overactivity seemed to obtain. They were characterized by discreet, deep pink, macules barely perceptibly raised, varying from the size of a pea to that of a quarter. They disappeared on pressure. Itching was intense. There was no scaling, weeping, or edema. In both cases, partial thyroidectomy was done. Upon the first post-operative day, a marked exacerbation of the rash occurred followed within the fourth day by a complete subsidence without return.

—Author's Abstract

(THYROID) Basal metabolism and its clinical application Hepburn (J S) & Eberhard (H M), J Am Inst Homeop (N York), 1921, 14, 231-237

The various methods for the determination of basal metabolism are described, and results obtained with the metabolimeter of Jones are reported. A case of hypothyroidism with a basal metabolic rate of -16.3% was restored to a normal rate by administration of desiccated thyroid. A case of hyperthyroidism had a rate of $+35.4\%$ after operation on the thyroid. Two weeks after x-ray treatment the rate had risen to $+58.7\%$, and it decreased to $+35.4\%$ at the end of another week. A second x-ray treatment was then given, 1 week later the rate was $+45.7\%$, at the end of a further period of 2 weeks it had decreased to $+17\%$. Hence exposure of the thyroid to the x-ray produced first an increase, then a gradual decrease in the basal metabolic rate.—Chem Abst, 15, 3868

Accelerated development of tadpoles after feeding with THYROID (Tets over de versnelde ontwikkeling van kikkerlarven onder den invloed van voeding met gl thyroidea) Heringa (G C), Nederl Tijdschr v Geneesk (Haarlem), 1921, 65, (II), 1930-1934

When thyroid is given to tadpoles metamorphosis is accelerated. If the region of the gills in control animals is compared to the same region in animals fed with thyroid it is found that the latter do not show typical epithelium. This epithelium, which is possessed of a glandular function, becomes atrophic in animals fed with thyroid. While thyroid feeding apparently accelerates metamorphosis the actual differentiation of the tissues is retarded. At a time when the control animal already has adult muscles the thyroid animal still has embryonal muscular tissue. The author compares these findings to those of Walter, who states that if after thyroidectomy a nerve is cut, neither degeneration nor regeneration of the nerve is seen.—J K

Concerning chemical heat regulation in THYROID-less rats (Über die chemische Warmeregulation schilddrüsenloser Ratten) Hildebrandt (F), Arch f exper Path u Pharmacol (Leipzig), 1921, 90, 330-335

Hildebrandt controverts the statement that the thyroid is of great importance in temperature regulation. He denies the presence of any difference as regards chemical heat regulation in normal and thyroidless rats.—W J A.

(THYROID) Modern surgical treatment of goiter (Ueber den gegenwärtigen Stand der operativen Behandlung des Kropfes) Hildebrand (O), Deutsche med Wchnschr (Berlin), 1922, 48, 16-17
Of technical interest.—J K

The THYROID question (Zur Kropffrage) Hotz (G), Schweiz med Wehnschr (Basle), 1921, 51, 1153-1155

Hotz points out that thyroid prophylaxis for children is a pressing necessity in his country and should be carried out on an extensive scale with governmental assistance. The writer describes the types in which iodides as prophylactic agents are beneficial and those in which harmful results are to be anticipated. The principal field for prophylaxis is in young children, especially among girls. In school children massive doses of iodides are not essential. In many instances goiters exist among all children of given families, the condition depending upon the state of thyroid function of the parent during pregnancy. Among older women, especially the hard working class, goiters are very prevalent and are associated with premature age. In such types the iodides are said to be very harmful, resulting in a depletion of body strength and the production of an artificial Basedow's disease. For such conditions partial bilateral thyroidectomy yields better results. Specific cases of the several types are included in the article.—C P McC

Sensitivity of THYROIDECTOMIZED animals to diphtheria bacilli and toxin (Sensibilité des animaux éthyroïdés envers les toxines et le Bacille diphtérique) Houssay (B A) & Sordelli (A), Compt rend Soc de biol (Paris), 1921, 85, 677-678

A brief note giving the results of many experiments. Thyroidectomized guinea pigs and rabbits have the same resistance as normal animals, except in the period of enfeeblement and cachexia, when the resistance diminishes.—T C B

Formation of antibodies in THYROIDECTOMIZED animals (Formation d'anticorps chez les animaux éthyroïdés) Houssay (B A) & Sordelli (A), Compt rend Soc de biol (Paris), 1921, 85, 679-680

A study of the production of antibodies in the rabbit, dog and horse, deprived of their thyroids. Various antigens were used. The results are difficult to explain and a general conclusion cannot be drawn. Thyroidectomy has no influence on the production of hemolysins and agglutinins. The case of antitoxin is complex. In the thyroidectomized rabbit and especially the horse, the production of diphtheria and tetanus antitoxin is feeble than in the controls, in the dog, on the contrary, it is better than in the controls. It will be necessary to ascertain if the difference is due to distinct diet, or to qualitative or quantitative differences in the protein ingested. It is also possible that extirpation of the thyroid modifies the skin or other organs, and thus influences the production of antitoxin.

THYROIDECTOMY in cattle (La thyroïdectomie chez les bovins) Hug (E), Compt rend Soc de biol (Paris), 1921, 85, 953-954

The thyroid was removed from 3 calves, two at the age of 2 months, and one at the age of 3 months. No symptoms were observed except a retardation of growth, they were inferior to the controls of the same age and race (short horns) in size and weight. The calcium of the blood was the same as in the controls. They were observed during 19 months.—T C B

(**THYROID**) The dependence of goiter incidence among recruits upon the median yearly temperature (*Über die Abhängigkeit des Kropfvorkommens bei Rekruten von der mittleren Jahrestemperatur*) Hunziker (H), Schweiz med Wchnschr (Basel), 1921, 51, 337-343

Hunziker in this publication extends his observation that goiter among army recruits is related to the variation of temperature in the various Swiss districts. Observations to the number of 1,235 were made in one series of 95 districts, and 247 distributed over 19 other separated districts. Investigations were made as to the effect of elevation, temperature, wind conditions, cloudiness, humidity, etc. Extensive tables are included by the author supplying precise data concerning these several investigations. No relation was established between goiter and cloudiness or barometric reading, but a definite relation was found between temperature and goiter and a less distinct relation between humidity and goiter. With reference to temperature Hunziker states that disabling goiter among recruits, as observed during the past thirteen years, was distributed over the country in a manner dependent upon the median annual temperature of the various districts. For northern Switzerland this is 7° C.—C P McC

Diagnosis of hypothyroidism Janney (N W), Cal State J Med, 1921, 19, 313

This article emphasizes the exact correlation of laboratory data with often inconspicuous clinical symptoms and signs necessary for the detection of latent cases of hypothyroidism. (See report in full "Concerning the Diagnosis and Treatment of Hypothyroidism,") N W Janney, M D, and H E Henderson, M D, Santa Barbara, Cal, Arch of Int Med (Chicago), 1920, 26, 297-318. The frequency of latent hypothyroidism is emphasized and the infrequency of typical myxedema and cretinism. Hypothyroidism may present clinical symptoms resembling neurasthenia, intestinal toxemia, arterio-sclerosis, the greatest aid to exact diagnosis and treatment being determinations of the metabolic rate.

The relation of the THYROID to irregularities of metamorphosis in amphibia Jensen (C O), Publication of the Royal Vet & Agricult Serum Laborat (Copenhagen), 1921, 72, 145-171

(Danish with English summary) The thyroid of axolotl (*Amblystoma mexicanum*) was studied before and after the period at which metamorphosis may occasionally take place in this form. The gland is not abnormal in early stages, but when the animal is six to nine months old, regressive changes take place in it. These are like the senile changes seen in the thyroids of old specimens of *Amblystoma punctatum*, and consist of epithelial atrophy with coalescence of neighboring follicles. Five cases of precocious metamorphosis have been observed by this author among larvae of *Bufo* and *Rana*. In two of these the thyroids were unusually large, while in the other three no hypertrophy of the gland was observed. The author gives no measurements of these precocious frogs, but the plates suggest that they are abnormally small, and it is possible that the thyroids were large in proportion to the size of the animals. In wintering larvae of *R. escuienta*, the follicles of the thyroids are considerably distended by colloid, and the epithelium is flattened. In giant larvae very large thyroids are found, but here again the author has not considered the abnormal size of the animals. The data presented are not sufficient to throw any great light on the relation of the thyroid to precocious or delayed metamorphosis except in the case of the axolotl —M M H

(**THYROID**) Partial metamorphosis in *Amblystoma mexicanum* Jensen (C O), Publication of the Royal Vet & Agricult Serum Laborat (Copenhagen), 1921, 74, 173-180, Compt rend Soc de biol (Paris), 1921, 84, 423-424

Intra-abdominal injection of iodocasein in an axolotl about three years old produced a partial metamorphosis. The resultant "demi-amblystoma" is like the adult form in shape, and in the character of the skin and eyelids. It has the tail, webbed feet, gill clefts and internal gill apparatus and the mouth of the larva —M M H

The **THYROID** gland and anomalies of metamorphosis in the Anura (La glande thyroïde et les anomalies de métamorphose chez les Anoures) Jensen (C O), Compt rend Soc de biol (Paris), 1921, 84, 948-949

Same data as those presented in the Danish paper already reviewed, without the plates —M M H

THYROID feeding of invertebrates (Ueber Schilddrüsenfütterung an Wirbellosen) Kahn (R H), Arch f d ges Physiol (Berlin), 1921, 192, 81-92

From experiments on the larvae of *Corethra plumicornis*, *Ecdyurus forcipula* and *Tenebrio molitor*, it is concluded that the characteristic actions on growth and differentiation produced by thyroid feeding on tadpoles are not produced in invertebrates

—A T C

A striking case of asymmetry in the **THYROID** region associated with the occurrence of a branchial cyst Kampmeier (O F), Anat Record (Phila), 1921, 22, 311-316

In an adult negro male it was discovered upon dissection that the left lobe of the thyroid and the isthmus were entirely lacking The right side was normal Associated with the absence of the left lobe, a cyst, apparently of branchial origin, was present —W J A

(**THYROID**) Treatment of goiter (Behandlung des Kropfes) Krecke (A), München med Wchnschr , 1921, 68, 1429-1430

Often the best effect is seen from sending a patient to a place free from goiter or from changing the origin of his drinking water Some kinds of diffuse goiters, especially in young girls, decrease in size when iodine is given In elderly people it is necessary to be careful with iodine, for it may cause loss of flesh and even Graves' disease When a patient complains of palpitations the administration of iodine must be stopped at once The same must be said of the administration of thyroid The author warns against the use of iodine ointments or x-rays, which both cause adhesions Operation is necessary when there are symptoms of thyrotoxicosis or when respiration becomes difficult In recent years mortality is somewhat higher than formerly because instead of a hemi-strumectomy the operation is performed on both sides The greatest dangers are tetany and paralysis of the nervus recurrens Contraindications are serious diseases of respiration or circulation Recurrences after operation are not rare —J K

(**THYROID**) Ether-oil colonic anesthesia in goiter surgery Lathrop (M), Am J Surg , Q Suppl Anesth (N Y), 1921, 35, 14-16

Attention is called to the fact that subjects of hyperthyroidism may be anesthetized in bed without apprehension or upset through the use of colonic injection of olive oil, ether, and paraldehyde (Gwathney) reinforced if desired by local anesthesia Favorable results in several hundred cases are reported —C R

(**THYROID**) Colloid goiter Latzel (R), Deutsche med Wchschr (Berlin), 1921, 47, 1282

Demonstration of a woman of 21, with a positive venous pulse and a colloid goiter Probably the goiter is situated between the jugular and subclavian veins and the large arteries, thus transmitting to the former the pulse of the latter —J K

(**THYROID**) Observations on certain types of toxic goiter Levinson (C G), Am J Surg (N Y), 1917, 31, 234-240

Several case reports illustrative of improvement after surgical intervention in thyrotoxicosis The author believes that exophthalmic goiter is always a surgical disease —C R

THYROID conservation after goiter operations (Zur Stumpfversorgung bei Kropfoperationen) Liek (E), Zentralbl f Chir (Leipzig), 1921, 48, 1656-1658 .

Of technical surgical interest —J K

Studies on compensatory hypertrophy of the THYROID gland
Loeb (L), J M Research (Boston), 1919, 40, 199-228

Previous investigators in this field have used dogs Loeb believes that dogs are too susceptible to hypertrophies of the thyroid gland to permit accurate conclusions In the experiments reported in this paper, he therefore, used guinea pigs as the experimental animals Loeb first made a careful study of the normal histology of the thyroid of the guinea pig, and describes it in detail He found that removal of from one-half to three-fourths of the entire thyroid gland did not result in hypertrophy of the remaining gland tissue After almost complete removal of the thyroid there was hypertrophy of the small fragments that had been left behind The histologic changes observed in these remnants are described fully Almost complete extirpation of the thyroid in a pregnant guinea pig need not interrupt the pregnancy, but in most cases the compensatory hypertrophy of the remaining gland tissue was retarded Complete thyroidectomy during pregnancy or before fertilization did not induce hypertrophy of the thyroid gland of the offspring

—J P S

Studies in Compensatory Hypertrophy of the THYROID Gland II

- (a) Hypertrophy in auto-transplants of the thyroid gland (b) Does a deficiency in organ function influence transplantability?
 - (c) Hypertrophy in multiple transplants of the thyroid gland
- Loeb (L), & Hesselberg (C), J M Research (Boston), 1919, 40, 265-288

In a large majority of cases conditions in the autotransplant and remnant of the extirpated gland are identical, in a few instances the hypertrophy is less marked in the autotransplants In remnants as well as in autotransplants, three periods, differing in the character of proliferation can be distinguished (a) the period of regenerative proliferation, (b) the period of proliferation due to early hypertrophy, and (c) the resting period A deficiency in functionally (metabolically) active tissues does not noticeably influence the processes in organization and especially in vascularization which determine the healing-in of the graft Compensatory hypertrophy may however, secondarily cause an enlargement of the blood vessels which supply the hypertrophic area The grafted lobes of thvroid in cases of multiple transplantations have the same fate as the corresponding tissue in cases of single transplantations, and the success of the transplantation does not depend upon the physio-

logic need in the organism of the specific function supplied by the transplanted tissue —J P S

Studies on Compensatory Hypertrophy of the THYROID Gland III

- (a) The Effect of homolotoxins on hypertrophy of the thyroid
 (b) Change in weight of the host as a factor in compensatory hypertrophy (c) Phagocytosis in hypertrophic thyroid gland
 Loeb (L), & Hesselberg (C), J M Research (Boston), 1920, 41, 283-303

A After homoiotransplantation of the thyroid gland following an almost complete extirpation of the thyroid host, hypertrophy of the transplant may occur. The frequency and in some cases also perhaps, the intensity of the hypertrophic changes are probably diminished in cases of homoiotransplantation as compared to autotransplantation. A mitotic proliferation is associated with the development of hypertrophy in the homoiotransplanted as well as in the autotransplanted glands. The authors believe that the results obtained are due to the interaction of two substances, (1) the growth substances calling forth hypertrophy of the thyroid gland, and (2) homolotoxins. These growth substances are not individual-specific, which is in accordance with the fact that hormones in general are not only not individual-specific, but not even species-specific. In general, the authors conclude, homolotoxins affect injuriously not only the ordinary regenerative reaction, such as we observe after transplantation, but that they likewise interfere in an unfavorable manner with the action of various growth substances, without, however, being able to overcome the latter entirely.

B The Authors advance the tentative conclusion that the occurrence of hypertrophy is usually associated with a greater gain in weight than lack of hypertrophy, and, conversely, that a gain in weight of the animals in which a great part of the thyroid had been extirpated is a factor more favorable for the development of hypertrophy than a loss of weight.

C After injury of the thyroid gland, particles of blood pigment may appear in the acinus cells as well as in phagocytes which are found in the lumen of the acini. These granules seem to persist longer in the acinus cells than in the lumen of the acini, they are especially prone to appear in hypertrophic cells, they are never seen in normal glands. The authors conclude that in this case they have to deal with phagocytic activity on the part of thyroid cells.

—J P S

Studies in compensatory hypertrophy of the THYROID gland IV

The influence of iodine on hypertrophy of the thyroid gland
 Loeb (L), J M Research (Boston), 1920, 41, 481-494

Loeb extirpated a quantity of thyroid gland in guinea pigs necessary to call forth compensatory hypertrophy. To the animals so

treated he gave iodine, either potassium iodide by mouth or subcutaneously, or iodine dissolved in sesame oil. He found indications that perhaps iodine preparations increase the hypertrophic changes occurring in the remnants of the gland. But Loeb admits that this cannot be stated definitely at the present time. It is rather contrary to the prevailing views in regard to the effect of iodine upon hypertrophy of the thyroid. The author's results also suggest that summer heat may be a factor which interferes with compensatory hypertrophy.—J P S

Studies on compensatory hypertrophy of the THYROID gland V
The effect of the administration of thyroid, THYMUS gland and tethelin and of a meat diet on hypertrophy of the thyroid gland in guinea pigs. Loeb (L), J M Research (Boston), 1920, 42, 77-89

Feeding guinea pigs with thyroid tablets greatly inhibits compensatory hypertrophy of the thyroid gland in guinea pigs.—J P S almost complete thyroidectomy. This effect is direct and specific, and is not due to the loss of weight induced by the feeding of the thyroid. Preparations of iodine given along with the thyroid did not counteract the effect of the tablets. Feeding the thymus gland did not prevent hypertrophy of the thyroid remnants. Repeated injections of tethelin did not noticeably influence the degree of hypertrophy of the thyroid remnants which follows almost complete thyroidectomy. A diet consisting chiefly, but not exclusively of meat did not produce hypertrophic changes in the thyroid gland, such a meat diet neither prevented nor noticeably increased compensatory hypertrophy of the thyroid gland in guinea pigs.

(THYROID) On differences in the results of various kinds of syngenesioplasmic transplantations in dependence upon the relationship between donor and host. Loeb (L), J M Research (Boston), 1920, 41, 305-325

Loeb studied the results of transplanting thyroid gland from mother to child, from child to mother and to brother or sister. Following transplantations two reactions take place, first, fibroblastic and vascular, and second, lymphocytic. These reactions appear to be the result of the formation of syngenesiotoxins. These toxins and the reactions which they stimulate, are strongest after transplantations from child to mother and weakest after transplantations to brother or sister, while transplantations from mother to child occupy an intermediate position. Loeb thinks that these experimental results may have a practical value in the selection of a donor for tissue grafting.—J P S

(THYROID) Treatment of Graves' disease with iodine (Morbus Basedowii und Jodtherapie). Loewy (A) & Zondek (A), Deutsche med Wchnschr (Berlin), 1921, 47, 1387-1389

Neilszer some time ago reported good results from very small doses of iodine in Graves' disease. Loewy and Zondek tried very small doses of KI with most brilliant success. The subjective feelings of the patients improve and they gained in weight. By studying the respiratory quotient they could prove that the intensity and rapidity of metabolism is largely diminished by this treatment. They advise to begin with 3 drops of a 5% solution of KI, three times daily and to increase the dose gradually until the patient complains of feeling worse again or till he begins to lose flesh when a smaller dose must be given.—J K

(**THYROID**) The value of anociation in goiter operations. Lower (W E), Am J Surg, Q Suppl Anesth (N Y), 1921, 35, 7-9

A brief exposition of "anoci-association" in thyroid surgery, including elimination of the patient's apprehension, narcotics before operation, nitrous oxide inhalation and local anesthesia to prevent apparent impulses reaching the brain. Preliminary ligation is urged as a general procedure.—C R

Carcinoma of the THYROID McWilliams (C A), Ann Surg (Phila), 1917, 65, 787

Report of an alleged instance of carcinoma of the thyroid gland in a girl 18 years of age, it had been present three years. Surgical removal was followed by recovery. There were no symptoms of hyperthyroidism.—J P S

(**THYROID**) Colloid goiter. Morf (P F), Surg Gyn and Obst (Chicago), 1918, 26, 360

Not of endocrine interest.—E N

Tuberculosis of the THYROID Mosiman (R E), Surg Gyn & Obst (Chicago), 1917, 24, 680-693. 4 photomicrographs

This article is a report of 9 cases of tuberculosis of the thyroid. Most of them were discovered accidentally in course of the routine microscopic examination of glands removed at operation. In all of these cases there was evidence of a primary focus of tuberculosis in some other part of the body, or a definite history of a prolonged exposure to the disease. The author therefore believes it is extremely doubtful if primary tuberculosis of the thyroid occurs. The tuberculous process was found associated with various physiological and pathological changes in the gland such as hyperplasia, pure colloid goiter, adenomatous goiters, and sarcomas.—J P S

A case of woody THYROIDITIS Nicholson (Daniel), Jour Can Med Assoc (Toronto), 1921, 11, 742-743

A woman, 38 years old, previously always well, suddenly developed severe headaches, chills, nightsweats and anorexia with pain in the thyroid region and a pulse of 160. She showed none of the classical eye symptoms of Graves' disease, but she had fine digital tremors. There was bilateral enlargement of the thyroid, each lobe being about the size of a hen's egg, very hard and easily defined. Carcinoma of the thyroid was diagnosed and the mass removed. The tumor consisted of very dense fibrous tissue stroma with yellowish areas at intervals, and a few cysts. Microscopically there was a typical picture of tuberculous granulation tissue. Fibrous elements predominated, clusters of round cells were seen, giant cells were very numerous, but there was no caseation. Many of the colloid spaces were destroyed. The pathological findings would seem to be of longer duration than could be accounted for by the patient's symptoms. The prognosis in this condition is excellent. Illustrated by half tone plate of a microscopic section.

—Author's Abst

(THYROID) Relation between the chloride content of the blood and its volume per cent of cells. Norgaard (A) & Gram (H C), J Biol Chem (Balt), 1921, 49, 263-278

Chloride content of blood corpuscles is nearly constant at 0.31 per cent. Plasma values are also constant at close to 0.61 per cent by the method described. The figures in cases of goiter do not differ from the normal.—F S H

The quantity of glycogen in the liver and muscles of THYROPARATHYROIDECTOMIZED animals (Sur la teneur en glycogène du foie et des muscles chez les animaux thyroparathyroïdectomisés) Parhon (M), Compt rend Soc de biol (Paris), 1920, 83, 140-142

We know from the work of others that there is a diminished assimilation of glucose in parathyroidectomized animals, but these results have been obtained by determining the sugar in the urine after the injection of glucose. The present paper deals with the amount of glycogen in the liver and muscles of thyroparathyroidectomized dogs, fed on known quantities of bread per kilo of body weight. Tables of results are given. From the tables it is evident that the liver and muscles of the experimental animals contain less glycogen than the normal controls, the diminution is much greater in the liver than in the muscles, because the liver furnishes the carbohydrate necessary for muscular energy. The parathyroid secretion restrains the consumption of carbohydrates in the organism, probably by diminishing the excitability of the muscles. It must have an important role in muscle tonus, for when it is absent carbohydrates are used in excess and muscle tonus profoundly disturbed.

—T C B

(THYROID) Prophylaxis of goiter (Prophylaxie du goitre) Roux (C), Rev méd de la Suisse Rom (Geneva), 1918, 38, 317-321

The paper is a plea for the prophylactic use of iodine as well as its therapeutic use. It is pointed out that while the etiology of goiter is unknown, there is now no question that the immediate cause of thyroid hyperplasia is an iodine deficiency. He also shows that there are no serious dangers from the minute doses that are needed and have been used in goiter prevention.—D M

(THYROID) Struma maligna Schädel, München med Wchnschr, 1921, 68, 1506

The author observed 15 malignant out of 450 goiters seen in clinics. In his private practice he saw 4 malignant cases. Of these 19, 14 were cancer, 4 sarcoma, 1 sarcomatocarcinoma. Malignant goiter nearly always begins as benign. The first symptoms of malignant degeneration are increased size and consistence, decreased movability and neuralgiform pains. Though the prognosis is very bad, the best results are obtained with x-ray treatment followed by operation. Malignant goiters almost never produce symptoms of hyperthyroidism.—J K

(THYROID) The sympathetic theory of Graves' disease (Zur Sympathicus theorie des Morbus Basedowi) Seitz (E), Zentralbl f inn Med (Leipzig), 1921, 42, 842-844

In studying the amount of blood sugar and its variations in Graves' disease the author comes to the conclusion that in diseases of the thyroid there exists often an increased irritability of the sympathetic. This is most marked in Graves' disease. A fortnight after the operation for Graves' disease the blood sugar and the tonus of the vegetative nervous system is normal. In some cases of colloid goiter, however, the sympathicotonia may be increased after the operation. As there are cases of Graves' disease without a disturbed function of the sympathetic Seitz believes that this disease has its primary seat in the thyroid. The study of the blood sugar is a good way to get information concerning the seriousness of the disorder. Surgical treatment of Graves' disease gives splendid results.—J K

(THYROID) Genesis of congenital infantile myxedema (Zur Genese des angeborene und infantilen Myxodems) Siegert, München med Wchnschr, 1921, 68, 997

It is possible that the anlage of the thyroid degenerates or that the normal organ undergoes degeneration. It has never been proved that there exist cases without an anlage of the thyroid.—J K

Clinical observations on 100 nitrous oxid-oxygen anesthesia in cases of HYPERTHYROIDISM Sise (L F), Am J Surg, Q Suppl Anesth (N Y), 1921, 35, 9-12

The author states that the addition of nitrous oxid-oxygen anesthesia to local anesthesia with preliminary narcosis reduced the incidence of shock, lowered respiration and pulse rate during a series of 100 thyroidectomies by Lehey, and he believes made post-operative thyroid "storm" less severe. A three per cent mortality is reported —C R

(**THYROID**) A case of hypothyrosis with symptoms resembling urticaria (Ein Fall von Hypothyreose mit urtikariaähnlichen Erscheinungen) Stemmer, München med Wchnschr, 1921, 68, 1405-1406

A woman of 22 suddenly showed a reddening and a swelling of the skin and mucous membranes. Hypophysis, ovary and adrenal substance were given without success. The sexual organs were hypoplastic. Thyroid gave good results —J K

(**THYROID**) Nonthyrototoxic goiter Slesinger (E G), Practitioner (Lond), 1921, 57, 355-366

The following elaborate classifications is introduced and upon it is based a clinical dissertation of considerable interest

Innocent Goiter

- 1 Parenchymatous goiter
 - Physiological
 - Toxic
 - Congenital
 - Acquired
- 2 Colloid goiter
 - Adenoma
 - Diffuse
 - Diffuse adenomatous
 - Cystic
 - Fibrous
 - Calcareous
 - Osseous
- 3 Foetal adenoma
- 4 Hyperplastic thyrotoxic goiter (Graves' disease)

Malignant Goiter

- 1 Epithelial tumours
 - Carcinoma
 - Malignant adenoma
 - Metastatic colloid goiter
 - Parastruma
 - Postbranchial goiter
 - Papilloma
 - Cancroid

- 2 Connective tissue tumours
 Sarcomata
 Endotheliomata
 Peritheliomata

Each of the above types is then described. The various pressure signs and symptoms are excellently reviewed. Finally the prophylactic surgery of long standing goiters in order to prevent malignancy is emphasized, especially in view of the almost invariably fatal prognosis when malignancy has once definitely begun.

—H L

(**THYROID**) "Forme fruste" der Myxoderm. Stransky (E), Wiener klin Wchnschr, 1921, 34, 575

Demonstration of a patient with a swollen face, thin hair, fragile nails, normal temperature and palpable thyroid. Now and then migraine-like headaches are experienced. Psychically the patient is dull, with now and then intervals in which she is very bright. She has been five times pregnant. The author considers this case as hypothyroidism. —J K

(**THYROID**) Congenital myxedema (Myxedema congenital). Talliens, Rev méd de la Suisse Rom (Geneva), 1918, 38, 268

This paper reports the case of an infant, aged five months, with the typical appearance of a myxedematous cretin. Skin thick and dry, tongue large, abdomen distended, umbilical hernia, hands and feet short and square, thyroid not palpable. At first the patient was treated with "panglandine" with little success, later desiccated thyroid 0.15 to 0.3 grams daily was given with good results both as regards physical and mental development. —D M

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Endocrinology

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DIABETES INSIPIDUS, ITS PATHOGENESIS AND THERAPEUTICS

THOR STENSTRÖM, M D

From the Medical Clinic, Lund, Sweden —Professor Karl Petré

As early as 1916 (1) I had an opportunity of demonstrating a case of diabetes insipidus before the Medical Society of Lund. Careful study of the case led to the conclusion that current views of the disease need revision. Diabetes insipidus is rare in this part of the country, and since the occasion mentioned only two cases have been admitted to the Clinic. The opportunity to study these cases was limited.

Diabetes insipidus, here defined by its most prominent symptom, a polyuria with no other noticeable changes in the urine, is a phenomenon of human pathology that has been recognized for a long time. However, until the researches of Tallqvist (2) and Meyer (3), 15-20 years ago, diabetes insipidus was but a common name for a group of diseases of the most varied etiology, in which the predominant symptom was merely an increased excretion of urine.

Tallqvist ascribed the polyuria of diabetes insipidus not to increased activity of the kidneys, but to lack of power on the part of the kidneys to secrete urine with normal NaCl and N percentage. Meyer also considers that in diabetes insipidus verus, as distinguished from the polyuria arising after a primary poly-

dipsia, there is present a loss of concentrating power for all the "hainfahigen Stoffen" collectively

Veil (4) has, however, lately denied the value of the tests which have hitherto been considered convincing for establishing the presence of a primary polyuria, viz, the obvious diminution in the quantity, but maintained concentration, of the urine when the saline and protein ingredients in the food are reduced, and, on the other hand, an increased diuresis—in this case also without any remarkably noteworthy increase in the concentration—after the introduction on a single occasion of a larger quantity of sodium chloride. According to his view, which is founded upon extremely interesting researches into which lack of space unfortunately forbids me to enter, it is only by a strict limitation of the supply of fluid, a thirst-experiment in other words, that it is possible to form an idea as to whether in a given case of "diabetes insipidus" there is any restriction in the concentrating power of the kidneys. The patient whom I had under observation has satisfied the requirements which Meyer and Veil formulated as decisive for the diagnosis of a true diabetes insipidus. The history of his disease offers nothing remarkable and can be told in a few words.

A man—Journ No 108, 1916—twenty years of age, with a clean health record and presenting no hereditary features of interest, experienced during the early days of October, 1915, a gradually increasing feeling of thirst. At the same time polyuria, but with no special urinary inconvenience noted. A careful and comprehensive objective examination revealed nothing of interest, excepting some ulcerations with abrupt margin in the gluteal region, on the thighs, and the shin of the right leg. The Wassermann reaction was positive in the blood serum. The cerebro-spinal fluid was not pathologically changed, and on the cranial skiagram nothing abnormal could with certainty be detected. The urine, which contained no abnormal constituents, was light in color and had a specific gravity of 1.002.

Before admission into the hospital the patient had lived on ordinary food. A reduction of albumen and salt in the diet brought about a considerable diminution in the secretion of urine (Table I). On a diet of unsalted butter, bread, gruel, pork (rib portion), vegetables, potatoes, apples, and 1 gm. of salt, the quantity of urine decreased from 11 or 12 to 8 or 9 litres, and further to 7 litres, when a few days later the gram of salt was omitted.

During the whole time the total concentration of the urine remained almost on the same level, the specific gravity being about 0.001 and the freezing-point depression showing values varying between 0.12 and 0.08. In a normal individual under a similar experiment the quantity of urine—independently of the reduction of albuminous and saline foodstuffs—would have remained on the whole at about the same level as before, while the concentration would have diminished. This difference already makes it plausible that an impaired power of concentration in the kidneys is present, a probability which experimental

evidence shows to be a demonstrable fact, as will appear from the following

On March 7 the patient was given in the course of the day 20 gm of sodium chloride, administered to him partly in his food, partly in teaspoonfuls dissolved in water, with the result that the quantity of urine increased from 6,300 c c during the preceding 24 hours to 8,110 c c, or nearly 2 litres (Table II) On the following days also the urine maintained a fairly high level—the day after, 7,500, and afterwards, 7,000 c c The concentration of the urine, on the other hand, was unchanged A distinct retention of the salt took place, and not until nearly a week after its introduction, when the 24-hour quantities had reached the same level as before the beginning of the experiment, could it be considered to be completely eliminated The accelerated diuresis during the period of March 8-12 also must in all probability be ascribed to the protracted excretion of the salt As soon as the organism had recovered its equilibrium in regard to sodium chloride, the urine decreased to the same quantity as before the introduction of the salt. An interesting observation is that the percentage of the sodium chloride rises during the first few days after its introduction, which, therefore, shows that the kidneys do not, as a rule, use their utmost capacity of concentration, but are able under certain conditions to present a greater The study of the various portions of urine during periods of 24 hours leads to the same view It appears, namely, that the morning urine presents a higher degree of concentration than the urine passed later in the day

On one occasion (9/1, 1916) the patient was rigorously restricted with regard to supply of liquid (1,500 c c) The low specific gravity (1 002) found in the urine during this day argues to some extent for the presence of a genuine diabetes insipidus On this day, as well as the following, when the patient by no slight exertion of will-power succeeded in limiting his intake of fluids, the specific gravity did not reach higher values than during the time when he took fluids *ad libitum* Even supposing that in the hourly testing of the urine during the "day of thirst" an increased concentration might have been found in some single portion, there can under no circumstances be any question of a considerable increase, inasmuch as in that case there would have appeared in some degree a rise in the specific gravity for the total 24 hours

On a later occasion—17/2, 1917—when the patient came back to the hospital to undergo treatment for syphilis, a regular thirst-experiment was undertaken With the usual diet he then passed a good 4 litres of urine with specific gravity 1 005 On 21/2, 1917, the patient from the time of awaking to 7 p m received only 500 c c of fluid The previous night he had received about 12 c c Further attempts to restrict the amount of fluid were frustrated by the patient's refusal to submit to the treatment The night urine amounted to 800 c c, in the daytime he passed 1,350 c c The specific gravity of the morning urine was 1 0085 and rose during the day to 1 0145 at most. The maximum concentration of NaCl and N amounted to 0 61 and 1 32 per cent respectively Of special interest is it to note that the specific gravity does not increase in uniform progression, but shows after 1 p m a distinct tendency to fall, and this in spite of the fact that the patient after 4 p m, by which time the quantity of liquid allowed had been consumed, was given nothing more to drink until 7 p m A particularly noteworthy fact is that the diminishing specific gravity is caused by a gradual reduction of the sodium chloride concentration Thus an impaired power of concentration is manifested also by this experiment.

Considering myself, therefore, fully justified in pronouncing the present case to be one of genuine diabetes insipidus—even in accordance with the demands made by Veil—I now revert to the discussion of the pathogenesis of this disease. The view maintained by Meyer that the essence of the disease is to be sought

TABLE I

Day	Diet	Urine						Blood	
		Quant per 24 Hours C C	Freez- ing Point °C	NaCl		N		NaCl %	Sugar %
				0/00	Total Quant Gm	0/00	Total Quant Gm		
1916 22/1	Bread, butter, milk, cream, 100 gm meat	11,400	-0 12	1 00	11 4	0 98	11 2	0 50	0 101
23/1		12,200	-0 12	1 82	9 8	1 26	15 1	0 51	0 112
24/1		12,000	-0 12	0 70	8 4	1 12	13 2	0 50	0 112
25/1	Unsalted butter, bread, gruel, pork (rib port), greens, potatoes, apples, salt 1 gm	11,200	-0 11	0 96	10 8	1 26	14 1	0 50	0 100
26/1		11,500	-0 11	0 90	10 4	0 98	11 5	0 49	0 100
27/1		9,500	-0 10	0 94	8 9	1 25	11 9	0 49	0 097
28/1	Salt etc	10,400	-0 12	0 70	7 3	0 70	7 3	0 50	0 089
29/1		9,800	-0 10	0 62	6 3	0 63	6 2	0 50	0 095
30/1		8,700	-0 09	1 17	10 2	0 70	6 1	0 48	0 122
31/1		9,200	-0 09	0 58	5 4	1 40	12 9	0 48	0 128
1/2		8,000	-0 09	0 47	3 7	0 70	5 6	0 47	0 109
2/2		7,500	-0 08	0 53	3 9	0 85	6 4	0 49	0 101
3/2		7,300	-0 08	0 58	4 3	0 85	6 2	0 49	0 107
4/2		7,300	-0 08	0 47	3 4	0 64	4 7	0 49	0 101
5/2		7,000	-0 08	0 47	3 3	1 68	11 0	0 49	0 095
6/2		7,200	-0 09	0 58	4 2	0 83	6 0	0 47	0 111

in a diminished "Gesamtleistung der Niere" proves on further investigation to be untenable. The nearest support for this view was in particular the observation that with an increased supply of albuminous food-stuffs the kidneys also reacted with an aug-

mented diuresis, but with no increase in concentration. Therefore, since the kidneys, according to this test, besides being insufficient for salt, were also inadequate for nitrogen—which, together with salt, mainly causes molecular concentration of the urine—

TABLE II

Day 1916	Urine						Blood		
	Quant per 24 Hours C C	Freez- ing Point, °C	NaCl		N		NaCl %	Sugar %	Re- marks
			0/00	Total Quant Gm	0/00	Total Quant Gm			
3/3	6,550	-0 11	0 64	4 2	0 84	5 5	0 48	0 112	Sodium chloride 20 gm
4/3	6,900	-0 12	0 61	4 2	0 84	5 8	0 49	0 101	
5/3	6,700	-0 11	0 89	6 0	0 99	6 6	0 49	0 100	
6/3	6,300	-0 11	0 83	5 3	0 99	6 2	0 50	0 121	
7/3	8,100	-0 12	0 82	6 6	0 70	5 7	0 49	0 113	
8/3	7,500	-0 13	1 40	10 5	0 71	5 3	0 49	0 109	
9/3	7,000	-0 12	1 16	8 1	0 56	3 9	0 50	0 101	
10/3	7,000	-0 13	1 05	7 4	0 70	4 9	0 49	0 103	
11/3	7,000	-0 12	1 05	7 4	1 12	7 8	0 50	0 113	
12/3	7,000	-0 14	1 17	8 2	1 12	7 8	0 49	0 105	
13/3	5,075	-0 13	0 99	6 0	0 98	5 0	0 50	0 117	
14/3	6,000	-0 13	0 76	4 6	1 13	6 1	0 50	0 109	

TABLE III 21/2, 1917 THIRST EXPERIMENT

	Quantity of Urine C C	Sp G	N %	NaCl %
7-8 a m	150	1 0085	0 29	0 41
8-10 "	350	1 0105	0 66	0 54
10-11 "	145	1 011	0 94	0 61
11-1 p m	145	1 0145	1 26	0 61
1-3 "	240	1 014	1 32	0 50
3-5 "	175	1 013	0 99	0 41
5-7 "	145	1 013	1 26	0 37
7-8 p m	165	1 009	0 42	0 26

the conclusion was very natural. Experiments with the use of phosphoric acid on the other hand produced greatly diverging results.

Do the experiments made by the earlier authors really prove that the kidneys in an individual with diabetes insipidus are incapable of eliminating N in a concentrated form, or is some other line of explanation possible? In order to obtain an answer to this question I have submitted the recorded experimental results to a searching scrutiny, and the verdict of this criticism is that there is no doubt that a greater supply of protein has, to a considerable degree, increased the diuresis without appreciably affecting the concentration. Hence this points to the acceptance of Tallqvist's and Meyer's opinion—but only upon a superficial

TABLE IV TALLQVIST

Date	Body Weight (Kg)	Total Amount of N	Quantities Eliminated						
			Urine					Faeces	Total N
			Quan- tity C C	Sp G	Freez- ing Point, °C	NaCl		N	
						0/00	Gm	Gm	
Jan	66 8	22 58	3,720	1 004	-0 30	0 52	1 92	0 73	10 77
22		22 58	4,900	1 005	-0 35	0 58	2 94	0 73	13 47
23		22 58	6,050	1 005	-0 31	0 58	3 51	0 73	15 85
24		22 58	6,420	1 005	-0 32	0 59	3 11	0 73	21 27
25		22 58	7,700	1 005	-0 32	0 61	4 70	0 73	19 21
26		22 58	6,425	1 004	-0 32	0 58	3 63	0 73	21 93
27		22 13	7,850	1 004	-0 29	0 58	4 55	0 73	24 28
28		22 13	8,500	1 004	-0 29	0 60	5 10	0 73	21 98
29		22 13	7,300	1 005	-0 36	0 60	4 38	0 73	22 63
30		22 13	6,700	1 005	-0 36	0 59	3 95	0 73	21 50
31	65 2	22 13							

view. The study of the published series of experiments in which estimations have been made both of the nitrogen and of the sodium chloride eliminated—I have been able to find no more than three—has shown that in every case *the increased supply of protein has brought about an accelerated elimination of sodium chloride*. I pass on immediately to a detailed examination of the particular researches.

Tallqvist was the first to test the capacity of the organism for eliminating nitrogen. The patient with whom he worked had for some time been placed on a certain standard diet, and was all at once given a considerable quantity of protein (22.58 gm

N), which was continued. It was then found that in proportion as the organism adjusted itself to N the quantity of urine gradually increased from 3,720 c c during the first day of experiment to 8,500 c c. At the same time the specific gravity remained unchanged at 1.004-1.005. The molecular concentration varied from -0.29° to -0.36° . I quote in Tallqvist's own words the conclusions at which he arrived from these researches: "Die Menge des Harns nimmt also zu, je nach dem der demselben mit der Nahrung zugeführte, Stickstoff immer nach und nach vollständig darin enthalten ist, und das ganze liefert einen treffenden Beweis für die grosse Rolle, welche die Menge der zur Ausscheidung bestimmten N-haltigen Produkte für die Harnabspaltung spielt."

Regarding the elimination of sodium chloride it is conspicuous that the percentage is maintained unchanged, or, if anything, there appears a slight increase. The total excretion of salt, therefore, increases considerably at the same time. I shall return to this observation.

Meyer has also adopted for his researches into diabetes insipidus a method similar to Tallqvist's. After the patient had been put on a strict diet for some time, he received an addition of 150 gm. of meat per 24 hours, which was continued for a week. On the day on which the alteration was effected, the quantity of urine increased from about $7\frac{1}{2}$ litres to 10,400 c c, and during the rest of the experimental period it amounted to 8.3-10.4 litres daily. The specific gravity presented but unimportant changes between 1.002-1.004, the freezing-point depression went down somewhat from -0.15° - -0.17° before the commencement of the experiment to -0.20° - -0.22° . Once it presented a value as low as -0.26° . On account of this reaction of the kidneys to the supply of protein, Meyer likewise concluded that these organs in a certain measure were powerless to eliminate a more concentrated nitrogenous urine.

The total elimination of sodium chloride, however, presented considerably heightened values in this case also, and that this is not an accident becomes evident from a further experiment with similar arrangements, in which as large quantities as 14 to 15 gm. NaCl were eliminated as against values of 7.4 gm. before the addition of meat.

Finally, a Swedish author, Kahlmeter (5), has made an experiment of the same kind with a somewhat different mode of procedure in a case of diabetes insipidus. In the morning 10 gm of urea were administered to his patient, who had already been stabilized some days previously with regard to nitrogenous constituents. As the table indicates, no increase in the specific gravity of the urine appears in this case either, while the quantity of urine, on the other hand, has increased perceptibly. The total quantity of NaCl eliminated appreciably exceeds the quantity eliminated during the 24 hours before and after the experi-

TABLE V E MEYER (Case I, Table II)

	Date	Urine C C	Sp G	Freezing Point, °C	NaCl		N Gm
					%	Gm	
Limited diet	6/ 7X	7,600	1 003	-0 17	0 086	6 52	6 01
	7/ 8	7,600	1 002	-0 15	0 056	4 26	7 34
	8/ 9	7,450	1 003	-0 17	0 043	3 20	7 50
+ 150 gm meat	9/10	10,400	1 002	-0 17	0 078	8 11	11 17
	10/11	10,400	1 004	-0 20	0 099	10 29	14 63
	11/12	10,180	1 004	-0 20	—	—	14 90
	12/13	9,270	1 002	-0 21	0 097	9 07	13 38
	13/14	8,800	1 002	-0 22	—	—	13 98
	14/15	8,300	1 003	-0 26	0 065	5 40	14 69
	15/16	10,000	1 002	-0 20	0 073	7 25	15 42
Limited diet	5/ 6XI	9,300	1 002	-0 17	0 100	9 30	8 07
	6/ 7	10,460	1 002	-0 15	0 070	7 32	8 05
	7/ 8	8,640	1 001	-0 15	0 084	7 26	6 70
	8/ 9	6,380	1 002	-0 16	0 060	4 03	6 07
+ 150 gm meat	9/10	11,400	1 002	-0 19	0 150	11 97	14 41
	10/11	11,040	1 002	-0 19	0 139	15 35	10 66
	11/12	10,480	1 002	-0 20	0 134	14 04	9 61

ment. The percentage of sodium chloride in the urine remained constantly at about the same level.

The observation that in all these three cases the percentage of the sodium chloride in the urine after the introduction of protein remains unchanged, while the total quantity of sodium chloride eliminated considerably increases, is worthy of close attention.

Is it not natural to conclude that it is the increased NaCl-elimination that causes the accelerated diuresis? Sodium chloride, as is well known, cannot in these cases be eliminated

from the kidneys in a concentrated form, and since the increased supply of protein involves an accelerated elimination of salt, the natural consequence is that the urine increases in quantity in proportion to the increased elimination of sodium chloride, so that the organism may be able to excrete the mobilized quantity of salt. The consequence of this is, of course, that all other constituents of the urine will be found in a more diluted form than before.

In order to obtain a conclusive reply to this question, I have for a long period placed my patient on a diet strictly reduced as to salt and later also as to protein food, whereupon as small

TABLE VI KAHLMETER

Day	Nutriment					Waste Products					
	Protein	N	Water	Quantity of Urine, C C	Sp G	NaCl		Urea		N	
						Gm	%	Gm	%	Gm	%
23/5	56	9.8	2,700	2,500	1.004	3.45	0.15	8.75	0.35	7.5	0.30
24/5	9 a.m.	10 gm per os	urea								
Time											
9-12 noon	—	—	—	400	1.005	0.60	0.15	1.2	0.30	1.7	0.42
12-3 p.m.	—	—	—	750	1.003	1.12	0.15	—	—	—	—
3-6 "	—	—	—	750	1.002	1.12	0.15	2.7	0.36	—	—
6-9 "	—	—	—	700	1.003	1.05	0.15	—	—	—	—
9-12 mid-night	—	—	—	825	1.002	1.22	0.15	2.9	0.35	2.7	0.34
12-3 a.m.	—	—	—	550	1.003	0.55	0.10	—	—	—	—
3-6 "	—	—	—	800	1.004	0.90	0.15	—	—	—	—
6-9 "	—	—	—	400	1.004	0.40	0.10	1.6	0.4	—	—
Total 24 hours	58	9.3	3,500	4,975	1.003	6.96	0.13	17.9	0.36	18.8	0.38
25/5	53	8.5	2,800	3,100	1.004	4.6	0.15	12.4	0.4	11.2	0.36

quantities as 1.5 to 3 gm sodium chloride were eliminated, after which I gave him an appreciable addition of protein food (300 gm meat, 3 eggs, and 100 gm cheese)

During this test the daily secretion of N rose to nearly 12 gm, as against about 4 gm during the preceding period. Nevertheless, the quantity of urine remained invariably at the same level, while the freezing-point depression, on the other hand, presented a decided fall from -0.14° - -0.17° before the commencement of the experiment down to -0.36° during its course.

Thus my researches have led to a result which diverges absolutely from the results of previous investigators and this divergence is in all probability due to the fact that the patient—

on account of the protracted reduction of salt before the experiment—had no reserves of sodium chloride. No mobilization of sodium chloride such as might affect the diuresis has appeared as a result of the increased supply of protein, as we have seen was the case in the experiments of the authors quoted. The moderate increase of the entire quantity of sodium chloride excreted is in my case not larger than is to be explained by the addition of salt which the patient received as the result of the change in diet.

TABLE VII AUTHOR'S EXPERIMENT

Day	Diet	Quantity of Urine per 24 Hours C C	Freezing Point, °C	N		NaCl	
				0/00	Gm	0/00	Gm
July 25	Fat, greens, potatoes, 150 gm bread	3,600	-0 17	1 40	5 04	0 59	2 12
26		4,000	-0 16	0 98	3 92	0 64	2 56
27		3,200	-0 15	0 98	3 14	0 64	2 05
28		3,400	-0 14	0 98	3 33	0 64	2 18
29		4,000	-0 15	1 12	4 48	0 88	3 52
30	300 gm meat, 3 eggs, 100 gm cheese	4,000	-0 21	1 40	5 60	0 88	3 52
31		4,000	-0 28	1 40	5 60	1 05	4 20
Aug 1		3,600	-0 30	2 24	8 06	0 82	2 95
2		3,400	-0 34	1 90	6 46	0 88	2 99
3		4,000	-0 32	2 80	11 20	0 82	3 28
4		4,000	-0 32	2 52	10 08	0 94	3 76
5		4,000	-0 34	2 94	11 76	0 99	3 96
6		4,000	-0 36	3 08	12 32	1 05	4 20
7		4,000	-0 36	2 66	10 64	0 99	3 96
8		4,000	-0 32	1 26	5 04	0 99	3 96
9		4,000	-0 28	2 24	8 96	0 94	3 76
10		4,000	-0 29	2 52	10 08	0 88	3 52
11		4,000	-0 30	2 52	10 08	1 05	4 20

Norgaard (6) describes a case of diabetes insipidus in which the daily quantity of urine was not "appreciably" increased after the introduction of 20 gm of urea. This state of affairs is not improbably to be ascribed to the "saltless" diet on which the patient had for some time been living and in consequence of which the organism had been freed from the greater part of its reserves of sodium chloride. The result was that this case dif-

ferred from Kahlmeter's in that the excretion of sodium chloride, too, was not "appreciably" increased

My conclusion is that the conflicting results to which my researches and those of previous investigators have led are due to differences in the mode of conducting the experiments. If a patient with a genuine diabetes insipidus has at his disposal considerable reserves of sodium chloride in the organism, an increased supply of protein causes an accelerated elimination of salt. But if he has previously been deprived of these reserves, as a result of a sufficient reduction of sodium chloride in the food, no increased quantity of NaCl will be excreted. The manner in which the kidneys react to the increase of protein varies according to the different conditions of experiment. In the first instance he responds with a markedly increased diuresis, but with maintained concentration of urine, in the second case he reacts in the same way as a normal individual, with maintained or but slightly increased quantity of urine and rising concentration.

The close analysis of previous experiments and of the results of my own researches seems to justify my question as to whether, on the whole, there is in genuine diabetes insipidus any impaired power of concentrating N or any reduced "Gesamtleistung der Niere". At all events, no tenable proof for this is yet forthcoming, although, of course, I do not propose to deny that such cases may occur. Veil, to judge by a short review of a paper read by him before the 32nd German Congress for Internal Medicine, 1920, seems now to divide cases of diabetes insipidus into two classes—those with increased, and those with diminished NaCl-percentage in the blood, hyper- and hypo-chloraemic forms respectively.

My view that only an impaired power of concentrating NaCl occurs is to some extent borne out, in the case examined by me, by the thirst-experiment. On the day when this was carried out my patient excreted N in a concentration up to 1.32 per cent, whereas the NaCl excretion, on the contrary, did not go higher than 0.61 per cent, with a further drop to 0.37 per cent in spite of a continued reduction of liquid by regular stages. Again, the N percentage remained at the same level (See Table III).

Two more cases of diabetes insipidus which I have examined in the Clinic point in the same direction, although—as I have

already hinted—the patients' short stay in the hospital and their unwillingness to lend themselves to the experiment frustrated investigations of a more lengthy and detailed character. In the first case, No 151/1917, when the concentration test was taken, the N-concentration reached—at a specific gravity of 1.017—a height of 1.11 per cent, while NaCl was not excreted in a higher concentration than 0.39 per cent, in the second case, No 534/1917, the NaCl percentage kept at about the level (0.35-0.40 per cent) which it had reached during the preceding night's reduction of fluid, while the N-concentration rose in slow but steady progression from 0.43 to 0.78 per cent. The patient's positive refusal to undergo further reduction of liquid terminated the examinations, from which still more obvious proof might otherwise have been forthcoming.

Concerning the etiology of the disease, a hypothesis—based on experiments with animals and on the results of certain clinical experiences—has been adopted, namely, that diabetes insipidus originates in a hypofunction of the posterior (intermediary) pituitary lobe. That this question, however, is by no means definitely settled becomes evident from the criticism to which the Swedish author, af Klercker (7), and others have subjected the collective demonstrations of this hypothesis.

It has been necessary to touch briefly upon this prominent question since the assumption of a pituitary etiology for the genesis of diabetes insipidus has led to substitutive therapeutics with extract from the posterior (intermediary) pituitary lobe in subcutaneous injection or with the substance from the pituitary in its entirety, administered per os. Thus Umber (8) quotes a case in which the symptoms of disease completely disappeared after repeated injections with pituitrin during one day, and the patient remained free from symptoms for the fortnight during which he remained under observation. Another patient whom Graul (9) had treated with pituitary injections on alternate days during a period of 16 days, afterwards came under supervision in hospital for the three following weeks, and then passed a quantity of urine not exceeding 2 litres per 24 hours.

It must, indeed, seem singular that a disease caused by an insufficiency of an endocrine gland should give place to stabilized

health, even after the supply of the missing secretion is discontinued. Such an occurrence seems rather to vitiate the theory. In practice, however, one must not deny the value of therapeutic means which have brought about such excellent results as the above-mentioned Motzfeldt's (10) method, applied with great success, of giving the patient every evening fresh or dried pituitary bodies as a result of which the thirst and necessity of urination during the night were diminished, also speaks in favor of the proposed treatment.

Therefore our decision at the Clinic to make an experiment on these lines should not seem surprising, and this all the more so as the symptoms of diabetes insipidus had shown no tendency to yield, in spite of the fact that the Wassermann reaction in accordance with the anti-syphilitic treatment had proved negative.

On March 13, our patient was given at an interval of three hours, at 8 and 11 a m, a subcutaneous injection of 10 c c pituitrin. The urine passed during the ensuing 24 hours amounted to 5,075 c c, as against 7,000 the preceding day and 6,000 and somewhat more the following days. Unfortunately, the injection was given before the extra dose of salt had been entirely eliminated, so that the quantity of urine passed during the 24 hours previous to the day of the experiment shows a higher figure than would otherwise have been the case. A distinct diminution of the diuresis can, however, be established, and this arresting power of pituitrin becomes still more evident from observations during the hours immediately after the injections (Table VIII). The urine was collected every hour, and during the two hours previous to the use of pituitrin amounted to 400 and 200 c c respectively, when it suddenly dropped to 40, and remained during the following hours, while the effect of the pituitrin still asserted itself at 20 c c. Afterwards a rise recommenced up to 300-400 c c. The diminution of the diuresis was still more marked when compared with a control experiment, in which the separate portions of urine, for a period analogous with the time of the experiment, remained on a level between the limits of 220 and 425 c c (Table IX). No increased diuresis is observed, such as Kahlmeter had in one case noticed after the effect of the pituitrin had ceased, and I quote as an instance hereof a synoptic table (X).

of later date, when pituitrin was administered For purposes of comparison it should be noticed that the urine during the night (7 p m to 7 a m) usually amounted to $1\frac{1}{2}$ -2 litres

Simultaneously with the diminution of the urine the molecular concentration presents a rise After a temporary decline of the freezing-point depression, as compared with the earlier

TABLE VIII

Time	Quantity of Urine, C C	Freezing Point, °C	N		NaCl		Sugar 0/00
			0/00	Gm	0/00	Gm	
6- 7 a m	400	-0 16	1 60	0 64	1 17	0 51	—
7- 8 "	220	-0 12	1 06	0 233	0 82	0 178	0 23
1 0 c c pituitrin							
8- 9 a m	40	-0 35	2 52	0 101	1 99	0 08	—
9-10 "	20	-0 87	5 82	0 116	4 68	0 094	—
10-11 "	20	-0 86	5 26	0 105	4 68	0 094	—
1 0 c c pituitrin							
11-12 noon	20	-0 74	5 74	0 115	3 51	0 07	1 9
12- 1 p m	18		6 52				—
1- 2 "	28	-0 99	6 52	0 183	6 55	0 183	—
2- 3 "	305	-0 12	1 12	0 341	1 3	0 397	—
3- 4 "	445	-0 10	0 81	0 35	0 64	0 285	0 21

TABLE IX

Test Experiment Time	Quantity of Urine, C C	Freezing Point, °C	N		NaCl		Sugar 0/00
			0/00	Gm	0/00	Gm	
6- 7 a m	220	-0 14	1 04	0 229	0 59	0 13	—
7- 8 "	280	-0 12	0 87	0 24	0 53	0 15	0 23
8- 9 "	400	-0 09	0 87	0 35	0 53	0 21	—
9-10 "	320	-0 08	0 95	0 30	0 47	0 15	—
10-11 "	340	-0 10	0 84	0 29	0 53	0 19	—
11-12 "	240	-0 10	0 87	0 21	0 70	0 17	0 18
12- 1 p m	250	-0 13	0 92	0 23	0 82	0 21	—
1- 2 "	425	-0 11	0 74	0 31	0 53	0 23	—
2- 3 "	365	-0 11	0 87	0 32	0 59	0 22	—

morning urine, a large increase took place after the injection While the test experiment with the different portions of urine presents values varying between -0.08° and -0.12° , the freezing-point depression has reached a maximum value of -0.99° at 2 p m (Table VIII)

With the increased total concentration the percentage of the NaCl and N secretion is augmented, but not in corresponding proportion as Norgaard found. A certain retention of these substances occurs.

A certain interest attaches to the observation that pituitrin causes an abnormal excretion of sugar, fixed on one occasion at 1.9 o/oo, and that is particularly remarkable when one considers that in normal individuals the subcutaneous injection of pituitrin as a rule has no such effect.

On three later occasions, commencing April 4 and 27 and May 4, the patient for a few days received pituitrin injections.

TABLE X.

Time	27 April	28 April	29 April	4 May	5 May	6 May	7 May
8 a m	C C 300	C C 250	C C 380	C C 240	C C 300	C C 400	C C 320
1 0 c c pituitrin							
9 a m	20	20	20	20	20	20	20
10 "	30	30	30	30	25	20	20
11 "	40	30	40	80	60	20	20
1 0 c c pituitrin							
12 noon	20	20	20	20	20	20	20
1 p m	20	20	20	20	20	20	20
2 "	20	20	20	20	20	20	20
3 "	20	20	20	20	20	20	100
4 "	20	40	20	20	20	20	200
5 "	30	40	30	20	20	20	50
6 "	60	240	150	100	100	120	50
7 "	60	100	200	100	150	120	40
Night Urine	1360	1870	1650	790	955	1280	990

in a similar way, the result being that the effect of the pituitrin in regard to the diminution of the diuresis was considerably more prominent than on the first occasion. The lowest quantity of urine per 24 hours on the respective occasions was 4,600, 2,000 and 1,300 c c, corresponding to 6,000, 6,000 and 5,200 c c per 24 hours before the injection. When the injection of pituitrin had been discontinued, the urine showed some increase after the period beginning April 4, but both after the single experiment and after the two following periods the diuresis continued to be smaller than before the experiment.

In regard to the effect of the pituitrin upon NaCl and N in the daily quantity of urine, it is conspicuous that no stability

can be noticed. The first and third experiments (March and April 27) show no increased percentage of NaCl excretion, although this is found on the two other occasions. The total quantity of NaCl remains approximately unchanged during the first two periods of experiment, but shows an obvious decrease during those of later date.

Generally speaking, a percentile increase in the excretion is to be observed, but the total quantity of N per 24 hours is nevertheless lower than before the pituitrin injections.

The effects of the pituitrin on the patient with diabetes insipidus examined by me may perhaps be summed up thus: the diuresis always presents a diminution and the molecular concentration in the urine shows a rise parallel with this and approximately proportional to the diminished quantity of urine. Sodium chloride and nitrogen, to judge from their total amounts, are on the whole eliminated in smaller quantities, even on the occasions when there is a considerable increase per cent in their excretion. No constant effect can be established.

My own experiments in regard to the value of pituitrin in the treatment of the diabetes insipidus case in question have thus yielded not altogether favorable results. In view of the experience thus attained, and with the foregoing discussion in the background, the opinion can hardly be considered exaggerated that this method of treatment by no means involves any therapeutic attack upon the original causes of the disease. In spite of the apparently good results shown in the cases adduced by Unger and Graul, and more recently by Schnabel and Gerhard (11), the majority of cases in the extant literature of the subject have only a transitory "success" to show, and I am skeptical as to the advisability of adopting the use of pituitrin as a general method of treatment. This standpoint may, in my opinion, be defended by calling attention to the far from desirable diminution of the excretion of sodium chloride which may take place during the pituitrin treatment. If, on the other hand, as was the case with the patient examined by Norgaard, an increase in the absolute excretion of NaCl is the consequence of the pituitrin injections, this method of treatment is probably worth trying. But with Motzfeldt I propose as a symptomatic method of treatment the introduction towards night-time of

pituitary substance. By this means my patient secured an obvious subjective relief from the otherwise somewhat troublesome feeling of thirst and the need of urinating during the night.

There remains the dietetic treatment. In order to reduce the patient's feeling of thirst and to save him the frequent urination, which during the night is particularly disturbing, it has hitherto been the general therapeutic rule to reduce as far as possible the use of saline and protein foodstuffs. Of Swedish authors, af Klercker, for instance, says that in the symptomatic treatment of the disease "the arrangement of a suitable and as far as possible non-saline and non-protein diet must be the chief object," and Hedenius remarks that "the essential point in the treatment is to try as far as possible to lessen the secretory work of the kidneys by diminishing the supply of salt and reducing the supply of protein to a bare minimum.

It goes without saying that such a diet must after some time become monotonous. And not only so, but the addition of vegetables, which must be made in consequence of the reduction of sodium chloride, has a still more troublesome effect upon the patient, it being a well-known fact that a vegetarian diet brings an increased demand for salt. However, the experience gained by my experiments makes it *now possible*—at least in cases similar to the one analysed by me—to *vary the diet somewhat by the introduction of a more protein food*, and it may even be questioned whether it be not advisable in these cases to introduce from the very beginning of the treatment a larger quantity of protein, in order the more rapidly to deprive the patient of his reserve fund of sodium chloride.

SUMMARY

The principle of treating diabetes insipidus has been to limit sodium chloride and protein because it is assumed that secretory power for NaCl and N is limited. Critical examination of the literature and personal experience fails to substantiate this as generally true. In the dietetic treatment only the sodium chloride need ordinarily be reduced. In certain cases it appears that permanent improvement has been attained by the administration of pituitrin. Principally on theoretical grounds it appears unjustifiable to resort to it uncritically in every case. Pituitrin injections raise the concentration of the urine simul-

taneously with diminution of the quantity secreted, thereby restoring the kidneys to a partially normal state. But the concentration does not in every case rise in proportion to the diminution of quantity, resulting in a certain retention of NaCl. In such cases pituitrin should not be used and before it is employed the foregoing principle should be considered. An illustrative case is reported

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A PSEUDOHERMAPHRITIC COCK

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The subject of this study was described as a hen that crowed and laid eggs but never brooded. Thinking that this might be a case of "masculismus" with altered endocrine function we secured the bird. It was a little larger than average, weighing 1950 gms. The plumage resembled closely that of a normal hen. It apparently was related to the race of Sebright Bantams. Like the cocks of this race, our animal had a thick and heavy comb—7 cm long and 2.5 cm wide. The wattles and ear appendages did not differ appreciably from those of a normal cock.

At necropsy the sub-peritoneal fat was found abundant. In front of the vertebral column, at the level of the genital glands, on the right side was seen an oval body, somewhat lobulated in appearance—2.75 cm long and nearly 2 cm wide. In form and color it resembled a testis, but its consistency was much firmer than that of a normal testis in this species.

On the left side was a tri-lobed body, the right portion of which was 3 cm long. This part was bounded by a horizontal portion, with a third part having nearly the same length. It was much lobulated and, in places, markedly granulated. In consistency, the body was as hard as cartilage and its color was bright yellow, that of the formation on the right side was grayish white. We believed the tri-lobed body to be a modified ovary, owing to the presence of a well developed oviduct similar to that of laying hens. But the consistency of the tri-lobed body was not that of the normal bird ovary and did not show any eggs.

There was a similar canal on the left side. Microscopic examination showed both to possess the characteristic structure of the oviduct in the laying hen. The accompanying photograph shows the genital glands and the excretory ducts of this bird.

The adrenals appeared microscopically and macroscopically normal

The thymus was well developed, forming a complete band on the right side and a band more or less interrupted on the left. The thyroids were the size of a lentil. The liver appeared rich in fat, while the pancreas was rather reduced, especially in the region of the tail.

In the organ on the right side, the microscope disclosed in places the structure of the testis of a normal cock, with well developed seminiferous tubules and active spermatogenesis. In other parts was seen a structure characterized by fairly thick,



almost hyalin, connective tissue rings resembling those of testicular sclerosis in man. These rings are certainly derived by the hyperplasia of the peritubular connective tissue. The cells of the tubules were almost completely lost at these places. It was the dense connective tissue which gave to the organ the hard consistency mentioned.

In general, the interstitial gland was only slightly developed throughout the organ.

In the tri-lobed structure of the left side, which we took for an ovary, microscopic examination failed to reveal any ovarian

characteristics In the microscopic study of the two structures, right and left, more than 3260 sections were examined, hence any ovarian tissue present would have been seen The tri-lobed body resembled a testis more or less modified according to the region examined Some regions possessed well developed seminiferous tubules showing spermatogenesis In other regions was seen a slight degree of peritubular sclerosis In places in both the right and left structures numerous foci of cellular infiltration having a lymphoid appearance were seen

Certain regions, especially the connective tissue rings, were thick and almost hyaline, like those of the structure on the right side In certain places, particularly where the sclerosed peritubular rings were the most noticeable, a well developed interstitial gland was observed, the cells of which were completely filled with lipid granules These were particularly noticeable in sections stained with Sudan-hematoxylin Similar granules were observed in the cellular rests occasionally found in the interior of the sclerosed rings In certain regions there were cords or masses of epithelial cells, more or less well circumscribed, but in which all evidence of spermatogenesis was absent

Finally, in other regions the epithelial cells were more or less broken up by new connective tissue containing numerous cellular forms, including fibroblasts

The surface of certain regions in the organ of the left side showed cystic formations of variable size, some of which occupied the greater part of a microscopic field (Zeiss ocular 4, objective A) These formations—which recall the retroperitoneal cysts observed in rare cases in man, and which seem to have genetic relations with the anlagen of the genital glands—contained an albuminous substance, staining as does the colloid of the thyroid, or the contents of the uniferous tubules in albuminuria

Nothing of particular interest was noted microscopically in the hypophysis, thymus, liver, spleen or pancreas

SUMMARY

The case of a cock is described the testicles of which had been modified by a pathological process and which possessed two structures having the appearance of the oviducts in the laying

hen (According to our observations there is a regression of the oviducts during brooding in connection with the endocrine modifications, which, according to our opinion, determine the brooding state) Since no signs of ovarian tissue were found, the "oviducts" are difficult to account for The endocrine organs other than the gonads appeared normal The case is to be regarded as one of pseudohermaphroditism

CLINICAL STUDY OF A PATIENT SUFFERING FROM
INTENSE THIRST AND POLYURIA (DIABETES IN-
SIPIDUS) AND PRESENTING X-RAY EVIDENCE
OF MALIGNANT PROCESSES IN THE CRA-
NIAL BONES, POSSIBLY LATE METAS-
TASES OF MAMMARY CARCINOMA

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Recently there came under our observation a patient who had developed intense thirst and polyuria, which seemed to be associated with the appearance of malignant metastases in the bones of the skull. The case would seem to be of sufficient importance to put on record.

ANAMNESIS

The patient, who was brought to us for consultation by her family physician, was a woman of 58 years, the wife of a well-to-do business man.

She complained chiefly of excessive thirst, of very frequent urination, of weakness, of peculiar morning vomiting and of marked disability in the lower part of the back.

The family history was negative except that one sister had died of metastases of a cancer of the breast.

The patient herself had ordinarily been well except for chronic constipation. She had had four children and three miscarriages, and had passed the menopause at 43 with no remarkable symptoms. At 48 the left breast was removed by a competent surgeon because of a tumor, supposed to be a carcinoma.

The present illness had its beginning seven months before consultation. The patient noticed pain in the back and in various joints, especially the shoulders, knees and hips, but there was neither redness nor swelling and the pain in the various joints was inconstant and variable. The development of bilateral sciatic pain forced the patient to remain in bed for a short time.

Simultaneously with the development of these symptoms referable to the locomotor system, there appeared intense thirst and frequent urination. There was also marked anorexia, slight nausea and some morning vomiting of mucoid froth.

Gradually the sciatica and joint pains grew less and the patient was able to get about, though she still suffered from marked disability of the back. The gastric symptoms, however, continued as did

the polydipsia and the polyuria. At times a little clotted blood appeared in the throat, apparently coming from the posterior nares. There were two attacks of diffuse erythema of the legs, each attack lasting a day or two, to be followed by scaling. Twice there was transient diplopia while motoring. There was weakness and much loss of weight. The patient stated that, at times, she voided more than a gallon of urine in twenty-four hours. There was some itching of the skin. There was no headache. All the teeth had been removed four months before consultation.

STATUS PRAESENS

Examination at the time of our consultation showed a pale, feeble woman, still well nourished despite much recent loss of weight. Pupils and eye muscles showed no abnormalities. Ears and hearing were normal. The tonsils were small, slightly irregular, and showed a few occluded crypts. There was no thyroid struma. A few small retrocervical glands could be felt, but otherwise there was no glandular enlargement. The scar of the left breast operation was in excellent condition. The lungs were negative. The heart was normal. The pulse rate was 96. The blood pressure measured 120 to 130 systolic and 80 diastolic. There was no appreciable thickening of the peripheral blood vessels. There was a little tendency to round back, and the movements of the whole spine were very stiffly carried out. The most discomfort appeared to be localized in the lumbar region. The abdomen showed nothing remarkable. The deep reflexes and abdominal reflexes were normal. The sign of Babinski was negative. Neither sciatic region was tender and Kernig's maneuver caused no unusual discomfort.

LABORATORY REPORTS

During the weeks just preceding consultation, numerous careful, special examinations had been made in the hope of throwing more light upon the condition. The main results of these tests follow.

Blood Examination Red blood cells, 3,752,000, hemoglobin, 75 per cent, white blood cells, 5,800, blood Wassermann, negative, blood sugar, 121 mg per cent, blood nitrogen, 30.5 mg per cent, blood creatinin, 15 mg per cent.

Urine Examination Sp gr, 1.002; acid, no albumin, no sugar, in the sediment no casts, but occasional pus cells were found. Tests of the urine were made repeatedly with negative results, except for persistently low specific gravity (usually about 1.002). The amounts of urine were always large for each twenty-four hours.

Examination of Stomach Contents Free HCl, 12 acidity per cent, total acid, 40 acidity per cent, lactic acid, absent. The stomach contents were examined on several different occasions, once small blood clots were present in the stomach washings.

Feccs Occult blood was found in the stool on one occasion
Cerebrospinal Fluid Clear, 5 cells, Wassermann reaction, negative, tests for globulin, negative

X-RAY STUDIES

Five months before our examination evidence of infectious arthritis of the thoracic and lumbar spine was visible in roentgenograms, but nothing further could be made out. Three weeks before consultation various long bones had been studied by means of the x-ray, on suspicion of a possible malignant condition, but nothing was found, and the arthritic changes in the spine were regarded as sufficient explanation of the symptoms in the back. The gastrointestinal tract had also been carefully studied roentgenologically, but no evidence of any lesion in the stomach or intestines beyond adhesions in the right upper quadrant of the abdomen was obtained.

NOSE AND THROAT EXAMINATION

An ulcer had been found on the left aspect of the nasal septum. It was believed that this might explain the occasional appearance of blood in the nasopharynx, the blood clots once found in the stomach content, and, perhaps, also the occult blood in the feces.

SUMMARY

On summing up the situation, the principal features were as follows:

- 1 Loss of weight and strength
- 2 Gastric symptoms, including nausea, morning vomiting and anorexia
- 3 Polyuria and polydipsia
- 4 Disability of the spine

Of these, the fourth was easily explicable, apparently, on the basis of x-ray findings of infectious arthritis of the spine. No local cause had been found for the gastric symptoms. The loss of weight and strength and the general appearance of the patient made one fearful of a malignant process somewhere in the body, but none had been revealed. The urinary studies, blood findings and blood pressure were all rather against the polyuria being a manifestation of chronic nephritis, and there was nothing to suggest that it was of hysterical origin.

EFFECT OF INJECTIONS OF PITUITRIN

It seemed best to investigate next the effects of pituitrin upon the polyuria. The amount of urine excreted during the twenty-four hours preceding was found to be 3,000 cc. One milligram of pitui-

tritin was injected, hypodermically, twice a day for two days. During the first twenty-four hours after injection the urinary output was 2,500 cc., the amount of water ingested 2,000 cc. During the second twenty-four hours the urinary output was 2,000 cc., and the amount of water ingested was the same. The nausea was definitely less and the nocturia was reduced to two urinations the first night of the test and to one the second night.

EYES AND EYE GROUNDS

The eye grounds were carefully examined and found to be perfectly healthy. Central vision was good. The fields of vision, however, showed marked contraction for form and for colors. The ophthalmologist's report reads: "Without knowing anything of the general complaint of the patient, the markedly contracted fields point strongly toward hysteria."

X-RAY FINDINGS IN THE SKULL

X-ray studies of the skull showed normal paranasal sinuses, including the sphenoidal sinus. The sella turcica was of the flat, open type with no sign of any destruction of the base, or of the clinoid processes. Scattered through the cranial bones, particularly in the parietal and frontal regions, there were numerous rarefied areas of bone destruction, showing no evidence of new bone formation, the process in the bones was apparently invasive in character, in every way resembling the changes in malignancy.

COURSE AND TERMINATION

The patient's condition changed but little while under our observation. The cutaneous itching was controlled by a mild carbolic ointment. The polyuria became less marked and required no further use of pituitrin. The gastric symptoms persisted. About two weeks after our examination the patient gradually became dull, then comatose, and died on the third day of the coma, according to the report of the family physician, with evidence of increased intracranial pressure.

DISCUSSION OF SPECIAL FEATURES

The case presents a number of interesting possibilities and problems.

(1) In the first place, what was the origin of the apparently malignant processes in the bones of the skull? The lesions were multiple and certainly metastatic in origin. Repeated careful search was made for a primary, malignant process in the body, none was found, though this does not, of course, exclude the existence of such a lesion. Can we connect the sup-

posed left breast cancer, removed ten years earlier, with these metastases? The possibility must, of course, be kept in mind. Ordinarily, we feel pretty safe, in a cancer case, if the patient is entirely well three years after operation, and after five years, one is accustomed to look upon the cancer as cured. Crouzon and others, however, have reported late multiple metastases in the brain in two cases after removal of the breast for cancer. In one of these, the metastases occurred eighteen years after, and, in the other, twenty years after operation. The interval in our case was ten years.

We know, also, that carcinoma of the breast is the commonest cause of bone metastases in women, just as carcinoma of the prostate is the commonest cause in men. The order of frequency of the bones showing such metastases in women is as follows: Ribs, thoracic spine, lumbar spine, ilia, femur, skull and humerus. In this connection, it may be said that we were a little suspicious of a malignant process in the lumbar spine, though at the time of the x-ray examination there was no visible evidence of it.

(2) It would seem highly probable that the intense thirst and the polyuria exhibited by the patient should be viewed as evidence of the existence of a mild diabetes insipidus. The patient said that she had frequently voided more than a gallon of urine in twenty-four hours, though even this is, of course, a small amount in comparison with the quantities passed in many of the reported cases of diabetes insipidus. Many such cases have certainly suffered from diseases of the pituitary gland or of the floor of the third ventricle in its neighborhood. In our case, it seems reasonable to infer the presence of a metastatic growth in the region of the pituitary or of the floor of the third ventricle. Negative x-ray findings in the region of the sella would be expected, unless the growth had been of sufficiently long standing to bring about bone destruction. Many of the reported cases of diabetes insipidus have shown tumors in the region of the pituitary when examined post mortem.

(3) Can our case be related to the remarkable condition recently reported by Christian? His case was an exceedingly interesting one, that of a child of five years presenting the symptom complex of (1) Extensive defects in the bones of

the skull, (2) exophthalmos, and (3) diabetes insipidus. There were also less marked defects in the pelvic bones. Christian cites two other cases showing similar bony defects in the skull, one was that of a young boy with dystrophia adiposogenitalis and exophthalmos, the other that of a girl of four years with exophthalmos and diabetes insipidus. In the latter case, the x-ray revealed a defect in the right ilium and a spindle-like thickening in the upper part of the right femur. These two cases cited by Christian had been reported by Schuller, and in both instances, basilar intracranial tumors presumably existed, basilar tumors would not account, however, for the areas of bone destruction seen in the cranium in both cases nor for the additional defects in the pelvis and femur seen in one of the cases, particularly since the physical condition of both children was too good to allow one to accept the theory of the existence of metastases. Christian believes that the bony defects in all three cases are to be explained by changes in the function of the pituitary gland.

It does not seem probable that our case falls in the group just cited, since the x-rays in our patient revealed irregular-shaped, scattered areas, suggestive of an invasive, destructive process, whereas in the three cases reviewed by Christian, the bony margins of the defects were very sharply and clearly defined.

CONCLUSIONS

In retrospect, we should be inclined to regard the case reported here as one of multiple, malignant metastases in the bones of the skull, at the base of the brain, and, possibly, also in the lumbar spine. It is probable that the involvement of the base of the brain affected the mechanism regulating water metabolism, so that symptoms of mild diabetes insipidus developed. The origin of the metastases is uncertain, but it is quite possible that they were secondary to the breast cancer removed ten years before.

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CHANGES PRODUCED IN THE LARVAL BRAIN OF *RANA PIPIENS* BY THYROID FEEDING

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LAWRENCE

During the past decade, numerous investigations have been carried on, which have demonstrated that a very definite relationship exists between the thyroid gland and body growth. By the pioneer work of Gudernatsch in the field of thyroid feeding of tadpole larvae, a beginning was made which has since been so extended by numerous investigators that the field covered has grown most extensive in scope. Allen, in connection with his experiments on thyroid removal, has shown that the brain of thyroidless tadpoles does not proceed to maturity, but retains the early larval form. It has been shown by Larson and Rogers, that there is a definite relationship existing between the thyroid gland and the anterior lobe of the hypophysis, since normal development and growth does not occur in the absence of either. Felix Adler and P. E. Smith have done valuable work along the same line, while Swingle has shown that thyroid feeding has no influence on the development of the gonads of tadpole larvae. However, thus far there seem to be on record few data concerning the effect of thyroid feeding or hyperthyroidism on the general structure of the brain.

Early in the fall of 1920, the writer began a series of thyroid feeding experiments for the purpose of ascertaining, if possible, the effect of hyperthyroidism on the general brain structure of the developing larvae of *Rana pipiens*. Measured from the tip of the snout to the cloacal opening, the tadpoles averaged about 8 mm. in body length at the beginning of the experiment. The material used for food was composed of one part of thyroid powder prepared by Armour & Co., two parts of dried clover leaves, and eight parts of flour, thoroughly mixed into a paste and dried in thin sheets. The control food was made in the same way, except for the absence of thyroid powder, for which powdered egg yolk was substituted to make up the deficiency in protein.

The tadpoles were carefully matched in size, half of each size being used as controls. The food was given in small quantities twice a day and water changed in the bowls at the same time. The feeding continued as long as there were any thyroid-fed tadpoles alive in the various lots, and whenever a thyroid-fed tadpole died, a control of the same lot was taken out and both preserved in formalin for dissection. The brain was dissected out under a binocular microscope, by means of very fine pointed forceps and needle scalpel. Body measurements were made as above indicated, with a small caliper and millimeter rule. Brain measurements were made with an eye piece micrometer.

As has been previously described by Gudernatsch, Swingle and others, no external changes take place for four or five days, then a very remarkable differentiation begins, which gradually increases with feeding. As Swingle (1918) has described these external changes fully, it will be unnecessary to discuss them further than to say that, by exceeding care, a few tadpoles were kept on a thyroid diet for 40 to 60 days, thus becoming almost completely metamorphosed.

In the spring of 1921, two more lots were started, one averaging 4 mm. in body length and the other averaging around 15 to 18 mm. These lots of nearly 50 each, were fed in the same way as those of the previous fall and with essentially the same results. The last series of feeding experiments was made during the summer of 1921 and in this work the tadpoles were matched very carefully as to size and the thyroid feeding pushed fairly rapidly. These tadpoles averaged from 12 to 15 mm. body length.

RESULTS

External Body Changes The general external changes were exactly the same as those found by other workers, hence it is unnecessary to describe them in detail. As the results in the various lots of tadpoles were compared, however, a few marked differences were seen. For example, the first lot, consisting of tadpoles of 8 or 9 mm. body length, showed themselves able to stand the thyroid feeding much better than those averaging only 4 to 6 mm., and they were able to progress much further than the latter toward complete metamorphosis before death. It was also shown that the tadpoles fed in the late fall were more resistant to the toxic action of the thyroid hormone than those

fed in the early summer, since the average length of life of the tadpoles fed thyroid in the winter was 26 days, while the average in the summer was only 8 days. Those fed in the summer also had a great deal higher rate of metamorphosis than those fed in the winter, for, although the average length of life of the two lots was markedly different, the extent of metamorphosis was very much the same, as shown by the external indices of body development.

This, then, seems to indicate two things: the seasonal factor affects the amount of thyroid a tadpole may consume before yielding to its toxic effect; second, the length of life of the thyroid-fed tadpole varies directly as the amount of body tissue at the outset of the experiment. The seasonal effect may be due to the accelerated metabolism during the summer months and the greatly increased glandular activity, all of which would result in an increased susceptibility to thyroid feeding. The relation to body size at the beginning of the experiment may be due to the fact that the increased nitrogen metabolism brought about by the thyroid hormone is more easily withstood in the case of the larger and older tadpoles. Perhaps reserve materials may be stored in the larger tadpole, which can be utilized in the formation of new features of metamorphosis. Certain it is, the more body substance present, the further the tadpole proceeds toward complete metamorphosis before death.

Brain Changes. Just as there is a difference in the extent of external change caused by the two factors of season and body size, so in the case of the brain structures, the extent of metamorphosis depends somewhat on the length of time the tadpoles are able to live and feed on thyroid, and on the season of the year. However, there is evident a uniformity of change, which, although more marked in those fed longest, is nevertheless present throughout the series.

Beginning at the cranial portion of the brain, it is found that the cerebral hemispheres in the average case assume a more blunt appearance and lengthen out into a form very similar to that found in the adult frog. The pineal body, instead of standing out clearly defined between the caudal curves of the two lobes, is almost completely imbedded in the tissues of the diencephalon. The diencephalon itself seems to be crowded in between the optic lobes and cerebral hemispheres in a very pecu-

lar fashion and is much shortened antero-posteriorly and broadened and extended laterally. The shortening, as shown by data, is 40.65 per cent, while the broadening amounts to 19.78 per cent.

The optic lobes, especially in those specimens nearly meta-

Tadpole Number	Body Length	Brain Length	Width at Cer. Hem.	Length of Dienceph.	Width of Dienceph.	Length of Fossa Rh.	Width of Fossa Rh.	Length of Ant. Lobe	Width of Ant. Lobe
C1	12.0	3.98	1.69	.96	1.44	1.67	.70	357	324
E2	12.0	3.74	1.49	.41	1.62	1.66	.20	239	324
C3	12.8	3.62	1.62	.76	1.25	1.67	.60	297	389
E4	12.5	3.74	1.20	.42	1.85	1.44	.30	238	320
C5	11.6	3.12	1.35	.68	1.06	1.44	.51	328	292
E6	10.0	3.13	1.35	.35	1.31	1.33	.36	296	324
C7	16.0	4.11	1.82	1.01	1.50	2.00	.77	357	390
E8	14.5	4.29	1.67	.47	1.91	1.10	.40	327	385
C9	15.0	3.68	1.69	.82	1.53	1.66	.77	356	390
E10	13.0	3.68	1.60	.29	1.87			356	356
C11	18.0	4.29	1.95	1.01	1.77	2.21	.81	356	485
E12	16.0	4.60	1.80	.56	1.86	1.77	1.10	354	452
C13	17.0	4.23	1.82	.96	1.62	1.94	.97	327	389
E14	13.8	4.29	1.80	.58	1.74	1.99	.40	350	325
C15	17.0	4.41	1.79	1.01	1.62	1.77	.91	356	480
E16	15.0	4.29	1.61	.58	1.74	1.79	.50	310	422
C17	16.0	3.74	1.69	.82	1.55	1.72	.71	302	324
E18	13.5	4.05	1.61	.35	1.74	1.77	.40	297	321
C19	16.3	3.80	1.62	.86	1.31	1.94	.81	297	324
E20	13.0	3.64	1.35	.35	1.62	1.39	.40	297	324
C21	15.5	3.68	1.62	.84	1.37	1.83	.85	290	320
E22	13.5	3.80	1.67	.47	1.74			324	385
C23	10.8	2.76	1.29	.64	.93	1.27	.64	327	324
E24	8.5	2.70	1.29	.29	1.31	1.27	.30	297	292
C25	15.4	3.86	1.51	.82	1.37	1.66	.71	327	356
E26	14.0	4.11	1.42	.37	1.56	1.38	.71	290	385
C27	9.0	2.01	1.26	.55	1.00	1.33	.50	297	260
E28	6.6	1.65	1.01	.29	.93	1.10	.55	155	164
	-2.0	+ .04	-.083	-.25	+ .22	-.22	-.14	-.07	0.4 Average Deviation
		1.76			19.78				Percentage Increase
	13.89		6.50	40.65		14.20	38.40	12.50	6.7 Percentage Decrease

Data compiled from lot fed during summer. C—Represents control tadpoles and E—represents thyroid fed tadpoles. All measurements given in millimeters.

morphosed by the thyroid feeding, appear very similar to those of the brain of an adult frog. The globular appearance of the early tadpole stages has entirely disappeared and a more triangular shape assumed as is shown in accompanying diagrams. The

lateral surfaces of the lobes are flattened perceptibly and sometimes a slight depression is formed on the ventral lateral surface (Fig B3), due to the pressure of the forming auditory capsule

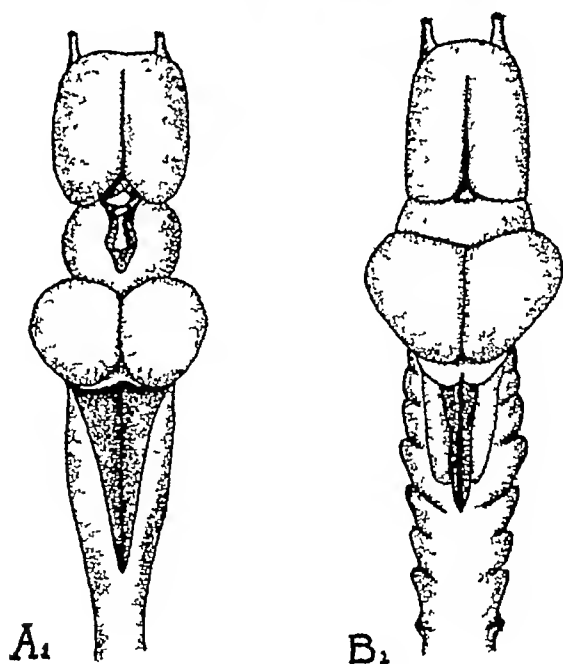
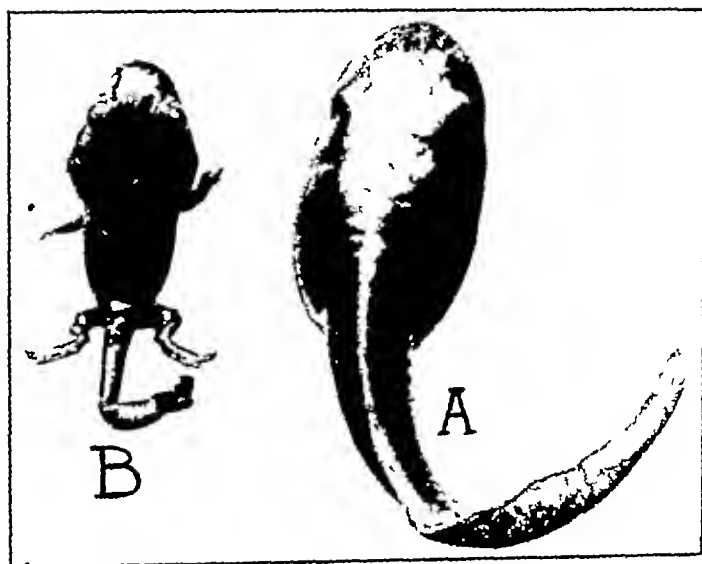
The cerebellum, which is very poorly developed in the adult frog and necessarily offers poor criteria for study, shows only a slight increase in thickness in the thyroid-fed tadpoles.

The fossa rhomboidalis presents a very remarkable differentiation, the lips of the ventricle are much closer together and the length of the opening is much shortened. This is especially striking since it corresponds so closely to the normal changes of metamorphosis, the decrease in width being 38.4 per cent and the decrease in length 14.2 per cent, as shown by the data. The medulla seems to be about the same size as that of the control tadpole, with, however, a vast difference in appearance. Instead of a smooth, even surface around the margin of the part, the medulla is broken on its surface into small furrows or ridges, which extend a considerable distance down the spinal cord. By careful dissection, it is shown that these ridges are due to the force exerted on the hind brain and medulla by the forming neural arches of the vertebrae. The probable explanation seems to be that while the average body length of the thyroid-fed tadpole is 13.89 per cent less than that of the control, the brain length is 1.76 per cent greater. We thus have two diametrically opposed factors, insufficient room is left between the developing neural arches for the expansion of the brain structure and pressure is brought to bear on the medulla, which results in the production of furrows or ridges.

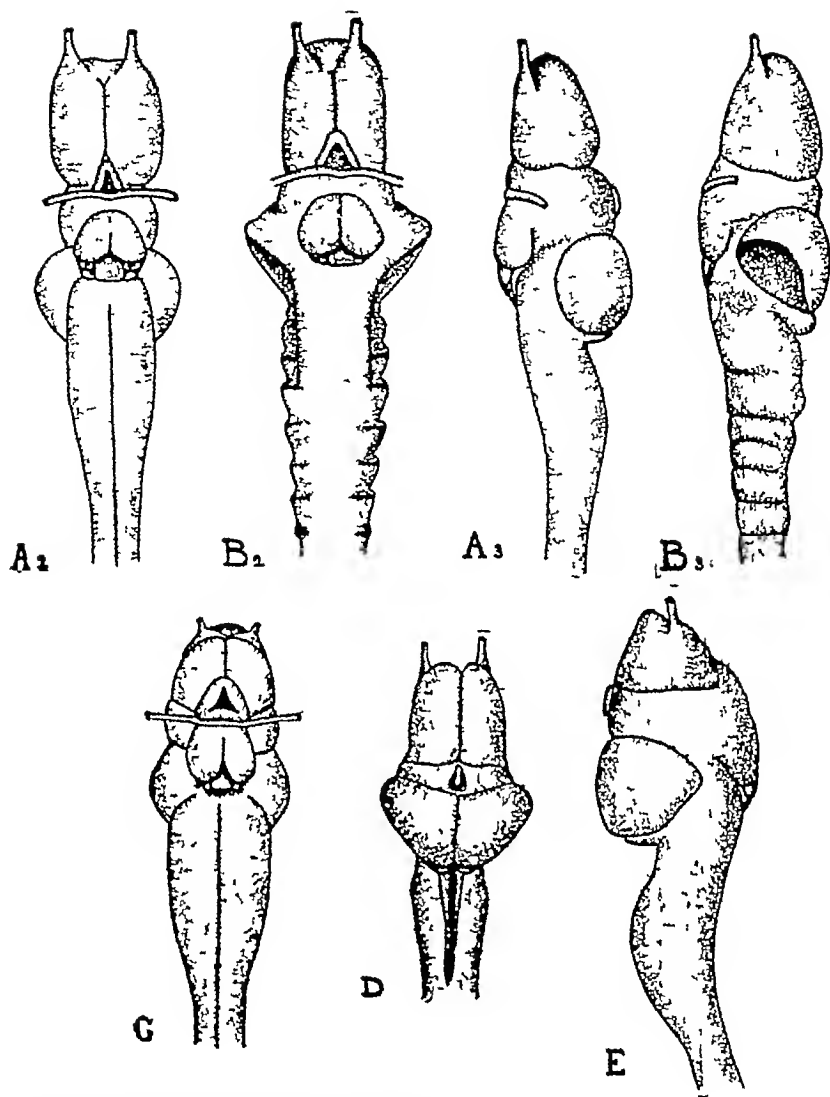
On the ventral side the same changes as indicated above are evident, with the addition of changes in the hypophysis and infundibulum, the infundibulum being slightly broadened laterally shortened antero-posteriorly. The posterior and intermediate lobes of the hypophysis are not noticeably changed, but the anterior lobe shows a decided decrease in size, as is indicated by the data. Only a cursory examination of the intermediate and posterior lobes was made, however.

DISCUSSION OF RESULTS

Without question, the majority of the changes brought about in the brain of the developing tadpole by thyroid feeding are those commonly seen during normal metamorphosis of a tadpole



A —Control tadpole, fed 40 days Body length 17.8 mm
 B —Thyroid fed tadpole, fed 40 days Body length 17 mm
 A1—Control tadpole brain, dorsal view Taken from tadpole A
 B1—Thyroid fed tadpole brain, dorsal view Taken from tadpole B



A2—Ventral view of same brain as A1

B2—Ventral view of same brain as B1

A3—Lateral view of same brain as A1

B3—Lateral view of same brain as B1

C —Lateral view of thyroid fed tadpole brain Taken from 8 mm tadpole fed in early spring Fed 17 days

D —Dorsal view of thyroid fed tadpole brain Taken from 12 mm tadpole fed in the early winter

E —Lateral view of thyroid fed brain Fed 18 days Note the bulged appearance of the medulla in the region of the fourth ventricle This was sometimes so marked that it could be seen from the outside with the naked eye It is due to the closing together of the lips of the fourth ventricle

larva This is especially true of the closing of the fossa rhomboidalis, the changed appearance of the cerebral hemispheres and optic lobes and the shortening of the diencephalon These facts show that thyroid feeding greatly accelerates the development of the brain, causing it to assume adult characteristics in a comparatively short time, as is clearly shown, for example, by the shortening of the diencephalon, which averages 40.65 per cent and the decrease in the width of opening of the fossa rhomboidalis, which averages 38.4 per cent in tadpoles fed only 7 to 11 days

The abnormal appearance of several portions of the brain appears to be due to the various rates of growth in the body of the tadpole Referring to the data, it is seen that the body length decreases under thyroid feeding while the brain length increases From some standpoints, it is most remarkable that while the body as a whole is steadily falling behind in size, the brain is increasing However, in the light of the numerous other changes produced when the rate of metamorphosis is accelerated by the thyroid feeding, it may be no more striking than the very rapid growth of the fore and hind limbs or any of the numerous other changes leading to maturity

As to the anterior lobe of the hypophysis, there seems to be some question on the interpretation of results Rogers (1918) shows that the anterior lobe of thyroidless tadpoles increases in size considerably beyond the normal He also makes the statement that the anterior lobe of his controls shows an increase in size, corresponding to the body development of the tadpole This seems to be the case from his data sheet, however, he made no very accurate study of these facts and obtained his results from but a few specimens The most important question arising is that regarding the change in size of the anterior lobe during normal metamorphosis If a decrease in size is common, then hyperthyroidism does nothing more than bring about the normal change of metamorphosis However, in view of the proven relationship existing between the anterior lobe of the hypophysis and the thyroid gland, it may be that the presence of an excess of thyroid hormone has lessened the necessity for the complete function of the anterior lobe and a slight degree of atrophy has resulted

SUMMARY

Armour's thyroid powder, mixed with powdered clover leaves and flour, was fed twice a day to a large series of frog tadpoles. Experimental and control tadpoles were carefully matched in size. The thyroid accelerated metamorphoses and also exerted a toxic effect, greatest in the summer, less in the spring and least in the autumn. The larger tadpoles survived longer and metamorphosed to greater extent than the smaller. In all parts of the brain of the thyroid fed tadpoles, adult characteristics were evident. The body length decreased 15.89% while the brain length increased 1.76%, the fossa rhomboidalis was much shortened, the cerebral hemispheres lost their globular form, the anterior lobe of the hypophysis was diminished in size, and other changes closely resembling those of normal metamorphosis were seen. Many striking abnormalities were produced in various parts of the brain, caused by pressure from surrounding structures. These were due to abnormal differential rates of growth.

In conclusion, I wish to acknowledge my indebtedness for the very great assistance and encouragement of Dr B. M. Allen of Kansas University, at whose suggestion this problem was undertaken.

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SOME FACTORS WHICH MODIFY THE EPINEPHRINE REACTION

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Oliver and Schafer (1) found that extracts of the suprarenal glands when injected intravenously produced a marked rise in blood pressure Elliott (2) studied the vascular response to epinephrine in great detail and found that the rise in blood pressure following the injection of epinephrine into an animal with the central nervous system destroyed was, within certain limits, directly proportional to the amount injected Investigations carried out by numerous workers demonstrated that the seat of action of epinephrine was chiefly, at any rate, the nerve endings of the sympathetic system, and that the effect of epinephrine was synonymous with stimulation of the sympathetic nerve supply The point of action of epinephrine was therefore considered to be entirely peripheral The effect of stimulation of the sympathetic nerve supply to any structure being known, the effect of epinephrine on any organ could be correctly predicted

That epinephrine, in addition to its well defined peripheral action, has a central action as well was suggested by the experiments of S J Meltzer and C Meltzer (3) They found that the intravenous injection of epinephrine caused definite vasoconstriction in the vessels of a rabbit's ear, but this constriction was followed immediately by dilation exceeding that which existed before the injection Langley (4) obtained similar results in the case of the submaxillary gland while Lewandowsky (5) found that the rise in systemic blood pressure in cats following the administration of epinephrine was frequently followed by a fall below the original level

Moore and Purinton (6) first demonstrated that the vascular response to very minute amounts of epinephrine was a definite fall in blood pressure, and this observation has been frequently confirmed by various workers in recent years

Dale found that the pressor response to a moderately strong dose of epinephrine was converted into a pure depressor effect if ergotoxin were administered between the epinephrine injections. He concluded that there are two sets of vasomotor fibres in the sympathetic—constrictors and dilators—the effect of ergotoxin being paralysis of the vaso-constrictor nerve ending. Epinephrine administration after ergotoxin caused a pure fall due to peripheral action on the vaso-dilator nerve endings.

Hoskins and McClure (8), working with pure “adrenalin” confirmed the earlier results of Moore and Purinton. They concluded that, as the effect of small doses of adrenalin was to cause a fall in blood pressure, the suprarenals do not ordinarily produce sufficient secretion to maintain any pressor influence.

Cannon and Lyman (9) found, after ligation of the coeliac axis, the superior and inferior mesenteric and the renal arteries that stimulation of the splanchnic caused a sheer fall in blood pressure. This they attributed to liberation of a small amount of epinephrine into the circulation.

These observers showed also that considerable modification of the vascular response to epinephrine could be produced by varying the rate of injection. A certain dose given very slowly might cause a pure fall in blood pressure, while the same dose injected quickly might be followed by a rise in blood pressure succeeded by a slight fall with return to normal shortly thereafter, or else by a pure rise with no successive fall. These authors also found that the blood pressure level previous to the administration of epinephrine was an important factor in determining the type of response to the drug. Thus they found that a dose of epinephrine which at first caused a pure fall in blood pressure, caused a rise only after the blood pressure had been lowered by pithing. They concluded that the depressor effect of epinephrine was not due either to central action or to stimulation of supposed vaso-dilator endings of the sympathetic but to the condition of the muscle of the vessel wall.

They held that vaso-dilatation resulted from epinephrine action when the muscle was tonically shortened, vaso-constriction when relaxed. Hartman (10) later found that effect of small doses of epinephrine given by intravenous injection was dilatation of the limb vessels and constriction of those in the

splanchnic area Hoskin, Gunning and Berry (11) showed that small doses of epinephrine produced constriction in the vessels of the cutaneous area and dilatation of the vessels of the limb muscles Hartman and Fraser (12) obtained dilatation in vessels of the splanchnic area and of the limb muscles by central action of epinephrine They attributed this result to direct stimulation of vaso-dilator cells, but they admit that dilatation may result by peripheral action as well Gruber (13) failed to obtain vaso-dilatation in limb vessels the nerves to which had been severed He attributed this result to loss of tonicity of the vessel walls, and is of the opinion that small doses of epinephrine cause dilatation by direct peripheral action

Hartman and Fraser (12) also demonstrated that the dilator response of the limb vessels to adrenalin was effected by temperature Thus they found that in a limb which had ceased dilating from artificial heat, the usual dose of adrenalin injected into the general circulation caused an increase in volume of the organ where previously the same dose of adrenalin produced either no effect or else constriction of the same

It is quite evident in the light of the experiments above referred to that the response to the administration of epinephrine as judged by the change observed to take place in systemic blood pressure is no indication of the exact nature of what is occurring It is rather the sum total of vascular changes in various parts Either constriction or dilatation of vessels may be the predominating effect, depending very largely upon the dosage employed Also constriction may result in one area and pure dilatation in another, while constriction followed by dilatation in any area is also a possibility

Collip (14) has recently demonstrated new methods of producing reversal of the effect of small doses of epinephrine Thus he found that a dose of epinephrine which causes a fall in systemic blood pressure can be converted into a pure rise, or into a slight rise followed by a slight fall, or else the fall will be greatly decreased by the injection of a variety of tissue extracts such as those prepared from heart, spleen, thyroid gland, suprarenal and pituitary bodies This reversal or antagonism of the depressor action of small doses of adrenalin by tissue extract is of short duration only, the depressor response returning within a few minutes after the administration

of the tissue extract It was found that similar reversal of the depressor action could be brought about by increasing the depth of anaesthesia Also on occasion the response of the systemic blood pressure to a definite dose of epinephrine can be altered by previous administration of sodium carbonate or acid phosphate, sodium carbonate tends to increase the pressor effect of epinephrine while acid phosphate tends to decrease it

Snyder and Andrus (15) obtained reversal of the effect of epinephrine on the isolated heart of the terrapin due to alteration of the hydrogen ion concentration of the perfusate Snyder and Campbell (16) have observed reversal of the constrictor effect of epinephrine on the perfused vessels of a frog following increase in the hydrogen ion concentration of the perfusate while the constrictor effect was increased by a decrease in the hydrogen ion concentration

The isolated uterus of certain animals is always inhibited by adrenalin when applied in very small amounts Collip (17) has shown that this inhibition reaction to epinephrine is antagonized by small amounts of tissue extract As the antagonism of the epinephrine reaction on certain isolated uteri by certain tissue extracts is very definitely a peripheral effect, it is quite possible that the antagonism or reversal of the depressor action of small doses of epinephrine on the systemic blood pressure by tissue extracts or by increasing degrees of anaesthesia is due to changes brought about in the periphery The writer inclines to the view of Dale (7) that vaso-dilator as well as vaso-constrictor nerve endings are stimulated by epinephrine The dilator endings are probably depressed by some constituent or constituents of tissue extracts with the result that the systemic blood pressure response to a small dose of epinephrine is definitely altered as above indicated The fact that a dose of epinephrine which will produce a pure fall in blood pressure in an animal under very light anaesthesia will produce a rise or a rise and slight fall when the anaesthetic is increased may be explained on the assumption that the vaso-dilator endings are more readily depressed by the anaesthetic than are the constrictors However, sufficient data have not as yet been obtained to enable one to explain in any definite manner just how these reversals of vascular reactions to epinephrine are produced

The cardiac response alone, for example, may be so altered under varied conditions as to play a large part in bringing about the observed results

That vaso-dilatation may be associated with central action of epinephrine is suggested by the demonstration by McGuigan (18) that the response of the systemic blood pressure to a definite dose of epinephrine is increased following the administration of just sufficient nicotine to block central impulses along sympathetic pathways

While the depressor action of a small dose of epinephrine may be completely reversed by increasing the depth of anaesthesia, it is also true that the pressor response to a large dose of epinephrine is decreased by anaesthesia*. This is due as McGuigan (18) points out to decreased irritability of the vaso-constrictor nerve endings, due to the increasing concentration of the anaesthetic in the blood stream

McGuigan (18) has shown that haemorrhage causes an augmentation of the pressor response to adrenalin. He has interpreted this effect as indicating an increased irritability of the sympathetic vaso-constrictor nerve endings in the vessel walls as a result of haemorrhage

The synergistic action of cocaine and epinephrine is still another example of the modification of the epinephrine reaction. This was first demonstrated by Frolich and Loewi (19). Recent experiments by Heinkeamp (20) demonstrate a synergistic action between morphine and epinephrine as regards their central action on medullary centres

It is now recognized as a result of the experiments of Levy (21) that the administration of epinephrine during chloroform anaesthesia is not without danger. He found that, if the animal were under light chloroform anaesthesia at the time of administration of the epinephrine, but had previously been deeply anaesthetised, the heart tended to go into fibrillation

The vascular response of an intact animal to epinephrine administration may be considerably modified by varying the mode of injection. Thus a dose of epinephrine which calls forth a decided pressor response when injected intravenously if given subcutaneously, may have little or no effect on the blood pressure. Becht (22) has shown that installation of epinephrine

* Unpublished results of Groot and Albrecht kindly furnished by Professor Hugh McGuigan

into the spinal canal produces a slight fall in blood pressure or else no effect. If, however, blood stained fluid exudes from the puncture needle prior to the injection a rise in blood pressure is frequently obtained. Variations in the response to epinephrine such as the above are probably related to the rate at which the active principle is introduced into the general circulation.

SUMMARY

A number of factors, which have been shown by various writers to produce a modification of the epinephrine reaction have been outlined.

The fact that very small doses of epinephrine cause a fall in blood pressure and not a rise has been emphasized.

Epinephrine may cause vaso-dilation in one area and vaso-constriction in another at the same time (Hartman and Fraser, Hoskins, Gunning and Berry).

A reversal of the depressor action of epinephrine may be accomplished by lowering the blood pressure level (Cannon and Lyman).

The pressor response of epinephrine is reversed by ergotoxin (Dale).

The reversal of the depressor action of epinephrine may be brought about by injection of tissue extract or by increasing the depth of anaesthesia (Collip).

Changes in hydrogen ion concentration may affect epinephrine response (Snyder, Campbell and Andrus, Collip).

The pressor response to epinephrine is decreased by anaesthesia (McGuigan).

The pressor response to epinephrine is increased following haemorrhage (McGuigan).

The mode of administration effects greatly the response to epinephrine.

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Book Reviews

LA CURE DE BOUCHARDAT ET LA TRAITEMENT DU DIABETE SUCRE (BOUCHARDAT'S TREATMENT OF DIABETES MELLITUS), by Prof F Rathery, Paris, 1920 Librairie Felix Alcan, 272 p

This exceedingly practical book first describes the old treatment of diabetes by Bouchardat. This is done in such an entertaining way that the book reads like a novel. It is remarkable that some principles earlier stated by Bouchardat are of fundamental importance in modern treatment. Thus he has been the first to ask regular analyses of urine, he also has warned against giving a diet, only because it has a certain amount of calories. He also has proved the importance of physical exercise in diabetes. The rest of the book is devoted to other methods of treatment, they are clearly and shortly described. A number of tables giving recipes for the preparation of various vegetables in the different seasons and of many other things important to medical men treating diabetes. The book can be warmly recommended to those wanting a practical book with a minimum of theory on diabetes.—J K

UEBER DEN JETZIGEN STAND DER DIABETESTHERAPIE (MODERN VIEWS ON THE TREATMENT OF DIABETES), by Prof Carl van Noorden, Munich & Wiesbaden, 1921 Verlag von J T Bergmann, 42 p

In this brochure the well known investigator describes the different treatments that recently have been recommended in diabetes. He himself recommends a combination of different systems

I Days with ordinary diabetes diet, with a protein content of 100-120 gram

II Days without meat and cheese with a maximum of 50 grams proteins. Potatoes and fruit must be given in amounts corresponding to 100 gram of bread

III Twice a fortnight a carbohydrate day is given. Bananas, apples, and rice, cooked with apples, are of more use than rice or oatmeal

IV Each carbohydrate day is followed by a fasting day or a day on which only vegetables are given

Carbohydrate treatment is indicated in acidosis. Though the administration of alkali is not so dangerous as Joslin believes, van Noorden recommends the use of as little alkali as possible

—J K

DIE UNTERBINDUNG AM HODEN UND DIE PUBERTATSDRUSENLEHRE
(THE LIGATION OF THE VAS DEFERENS AND THE THEORY OF A
PUBERTY GLAND), by Dr Hans Tiedje, Jena, 1921 Verlag,
von Gustav Fischer, 26 p

In this small brochure Tiedje describes his experiments on "rejuvenation" in guinea pigs. When one vas deferens is ligated and the other testicle removed in a young animal the remaining testicle develops normally. In older animals the testicle first atrophies, but later shows complete regeneration. In both young and old animals a spermatocele is generally formed. The same results are seen when both vasa deferentia are ligated. When one vas deferens is ligated and the other testicle is not removed the first testis atrophies, while the second shows a compensatory hypertrophy. The author holds that the interstitial cells are of great importance as organs regulating the nutrition of the testicle. He cannot, however, confirm Steinach's theory, by which the interstitial cells are considered to constitute a special gland having a definite endocrine function.—J K

BEITRAG ZUR ATROPHIE DES MENSCHLICHEN HODENS (STUDIES ON
THE ATROPHY OF THE HUMAN TESTICLE), by Dr K Goette,
Jena, 1921 Verlag von Gustav Fischer, 26 p

It is well known that different influences may cause an atrophy of the testicles. Poisons (alcohol), physical influences (x-rays), acute and chronic disease, all may have the same effect. Even when examined histologically the atrophic testicle shows the same picture, whether it is caused by x-rays, by alcohol or by some disease. The atrophy is a primary lesion of the seminal epithelium. The intensity of the atrophy depends on the time, during which the noxious influence lasted and on the general condition of the body. The formation of sperm is much less disturbed in acute disease than in chronic. Whether psychical and physical exertion have an influence on spermatogenesis is not known. This small brochure may be recommended to those making a special study of the gonads and their function.—J K

UEBER DIE RUSSISCH-RUMANISCHE KASTRATENSEKTE DER SKOPTZEN
(CONCERNING THE RUSSIAN-ROUMANIAN CASTRATED SECT OF
SKOPTZIES), by Dr Walter Koch, Jena, 1921 Verlag von
Gustav Fischer, 38 p

The Skoptzies are a religious sect living in Russia and Roumania. Their religion prescribes that male individuals be castrated. They distinguish between the "great operation" when penis and testicles are removed and the "little one" when only the testicles are cut away. Though several authors, notably Pelikan, Tandler and Grosz, and Pittard, have devoted much

labor to the study of this sect, much remains unknown Koch was able to study certain individuals of the sect during the German occupation of Roumania and he presents his results in this little book, which is enhanced by excellent photographs

In all cases examined the author found a pale skin, abundant hair of the head, scanty beard, few hairs on the body and in the axillae, female type of pubes, a wrinkled face, small lymphatic apparatus in the throat, small thyroid and long extremities Koch distinguishes four types of Skoptzies (7) ordinary type with long extremities, (2) type with giantism, (3) type with acromegaly, (4) type with hypophyseal adiposity The type seems to depend upon the age at which the operation is carried out The first type shows a normal sella turcica, in the second the sella seems to be enlarged In the third class the sella is much larger than normally Other abnormalities also are apparent in the skull

The author has carried out exact measurements of the different indices of the body The book must be considered of

ABDOMINAL PAIN Prof Dr Norbert Ortner, Vienna Tr by William A Brams and Alfred P Luger New York, 1922
Rebman Co 362 p 8°

The book is of interest to endocrinologists in that it includes brief discussions of pain associated with some of the endocrinopathies —R G H

KORPERBAU UND CHARAKTER. UNTERSUCHUNGEN ZUM KONSTITUTIONSPROBLEM UND ZUR LEHRE VON DEN TEMPERAMENTEN
Dr Ernst Kretschmer 1921 Julius Springer Berlin
192 p 31 pl

This monograph discusses in an interesting manner the apparent correlation between the various types of body form and the mental and psychic attributes The point of view is that of the psychiatrist and the examples cited are taken from psychiatric practice The evident abnormalities in function of the endocrine glands associated with the specific types discussed are brought out Temperament is considered as a matter of humoral or blood chemistry, the body representative of which is the brain-endocrine gland system The publication can be recommended to both the endocrinologist and the psychiatrist —F S H

THE AUTONOMIC NERVOUS SYSTEM J N Langley Cambridge,
1921 W Heffer & Sons, Ltd 80 p

Reviewed by Prof Sherrington in *Physiol Abst*, 1922, 6,
650

HORMONES AND HEREDITY A discussion of the evolution of adaptations and the evolution of species J T Cunningham.
London, 1921 Constable & Co, Ltd 246 p

After an introduction giving a historical survey of theories or suggestions of chemical influence in heredity, there follow chapters on classification and adaption, mendelism and the heredity of sex, influence of hormones on development of somatic sex characters, origin of somatic sex characters in evolution, mammalian sexual characters, evidence opposed to the hormone theory, origin of non-sexual characters, the phenomena of mutation, metamorphosis and recapitulation.

Cunningham believes that there are two distinct kinds of characters in all organisms, namely, those of somatogenic origin and those of gametogenic origin. Somatic modifications by means of hormones affect the determinants in the gametes. His theory supposes that every part of the body gives off special substances which have a special effect on the corresponding parts of the chromosomes. He even suggests that bones of different parts of the body give off different hormones. In discussing the development of the antlers of the stag it is supposed that an exostosis formed on the frontal bone as a result of repeated mechanical stimulation, due to the butting of stags, gives off an increased quantity of intermediate waste products of the same kind as the tissues from which it arose gave off before. These products act as a hormone on the gametocytes, stimulating the factors which in the next generation would control the development of the frontal bone and adjacent tissues. There are two hormone actions, the centripetal from the hypertrophic tissue to the corresponding factor in the gametocytes and the centrifugal from the testes to the tissue of the antler or other organ concerned.

Cunningham uses the term hormone in Starling's original sense, and includes all kinds of products of metabolism in the category. He argues that if the intestinal glands can produce an internal secretion, so also can other tissues. It is true that Starling originally referred to CO_2 as a hormone. We are not in a position to deny that all products of metabolism have an influence on the economy. On the other hand the majority of investigators at the present time do not admit that we have any evidence that such is the case.

The author believes in the inheritance of acquired characters. "There exists very good evidence that modifications due to external stimulus do not perish with the individual, but are in some degree handed on to succeeding generations."

The book is well written and beautifully illustrated —S V

THE VITAMINES H C Sherman and S L Smith N Y, 1922
The Chemical Catalog Co 273 p 8°, 3 pl

While vitamins are, so far as known, not internal secretions, endocrinologists, no doubt, in view of their interest in metabo-

ism, will be largely interested in this book. It takes up the history of vitamins and then treats successively of vitamins, A, B and C. A final chapter is devoted to vitamins in the problem of food supply. The evidence is succinctly but readably presented. The book closes with a valuable twenty-seven page bibliography.

—R G H

LOS MECANISMOS DE CORRELACIÓN FISIOLÓGICA. Augusto Pi Suñer. Barcelona, 1921. P. Salvat. 299 p. 8°

The book comprises a series of eighteen lectures delivered before the Faculty of Medical Sciences of Buenos Aires in 1919. As suggested by the title, the author takes up the various mechanisms by which physiological unity is attained. Cellular as well as nervous and hormone correlations are considered. Endocrinologists who are able to read Spanish will find the book an interesting exposition of the fundamental philosophy of their problems.—R G H

THE MORPHOLOGIC ASPECT OF INTELLIGENCE. Sante Naccarati. Columbia University Contributions to Philosophy and Psychology, Vol 27, No 2. N Y, 1921. 44 p. 8°

The book comprises a terse presentation of certain anthropologic and psychologic data from which the author draws various deductions of interest to the endocrinologist. Among the three morphologic types differentiated by Viola, viz, the microsplanchnic, the normosplanchnic and the macrosplanchnic, the microsplanchnic gives the more intelligent units. Normosplanchnics represent all degrees of intelligence. Macrosplanchnics, while representing a less intelligent group, individually may be as intelligent as any other type. The microsplanchnic type is mentally hyperevolute. This fact constitutes another proof in support of Viola's thesis that the macrosplanchnic type and not the microsplanchnic is an infantile type and therefore retarded in development. The microsplanchnic type corresponds to the hyperthyroid type, namely, that marked by a constitutionally hyperactive thyroid, an "Oithoplasic hyperthyroidism" (Pende), or a "Hyperthyroid temperament" (Levi and Rothschild). The morphologic type is the outcome of hereditary and accidental factors. Hormonic actions, which influence the physical and mental growth, the metabolism, and the nervous reactions, are in part responsible for the individual differences in the same family and in the same ethnic group. During the prenatal life and during infancy and the adolescent period, environment, diseases, traumata (physical and moral), improper diet, etc., may affect the function of one or more endocrine glands, and thus produce morphologic deviations which are usually accompanied by

mental deficiencies or gains on account of interrelations existing between the morphoregulator and the neuroregulator hormones
—R G H

STUDIES IN DEFICIENCY DISEASE Robert McCarrison, London, 1921 Henry Frowde and Hodder and Stoughton 270 p

For review see Am J M Sc, 1922, 163, 440-441 The monograph apparently is a compilation of the author's valuable studies previously published in the periodical literature Many of the data are of interest to endocrinologists They have appeared or will appear in this Journal in abstracts of the original articles —R G H

EPREUVE DE GOESCH Sigismond Bloch Paris, 1921 Vigot Frères 77 p 8°

Bloch reports in some detail the results of the Goetsch epinephrin test in a variety of clinical conditions in forty-eight subjects Definitely positive results were obtained in two cases of goitre—toxic and exophthalmic—one case of pluriglandular insufficiency, six of infection, two of diabetes and one of pregnancy Partially positive reactions were seen in three cases of Graves' disease, one of infantile myxedema, under thyroid treatment, three of infection, two of diabetes and one of chronic alcoholism Negative tests were obtained in twenty-two cases These included two of "Basedowified" goitre, one of five years' standing and the other in a pregnant woman, one doubtful case of Graves' disease, one of myxedema, six acute infections, five chronic infections, one chronic alcoholism, one dysenteriform colitis, one mitral regurgitation, one myopathy, three infantilism The author was impressed with the fact that cases taken at random in the great majority of instances give negative tests and that the positive tests are mostly obtained in cases in which thyroid involvement is common or essential On the whole, the test is regarded as valuable —R G H

THE JOURNAL OF BIOCHEMISTRY Motofujicho, Hongo, Tokyo, Japan Editor-in-chief, Prof Samuro Kakiuchi Vol 1, No 1, January, 1922

A new journal devoted to publication of work by Japanese investigators Articles are published in English, French and German, predominantly, but any language written in Roman characters is acceptable

THE JOURNAL OF METABOLIC RESEARCH Vol 1, No 1 Jan, 1922

A new journal devoted to the publication of original investigations in the field of metabolism Edited by Frederick M Allen Published monthly by "The Physiatrie Institute," Morristown, N J —R G H

Abstract Department

Clinical considerations of some cases of ACROMEGALY (Consideraciones clinicas sobre algunos casos de acromegalia) Martinez (G N) & Moyano (J J), Rev del Circulo méd de Cordoba, 1921, 9,—(Nos 5, 6, 7, 8)

This article gives an account of three cases of acromegaly observed at different periods of life, one in youth (24 years), the other two in maturity (51 and 61 years, respectively) All three showed typical manifestations of diabetes insipidus and latent or evident bitemporal hemianopsia In two cases radiographs disclosed enlargement of the sella turcica There was perfect and even augmented carbohydrate tolerance—B A H

(ADRENALS) Hyperchlorhydria in childhood Berman (L), New York M J, 1921 114, 226-228

The occurrence of hyperchlorhydria is commonly produced in a certain class or type of children by irritating foods Such children are generally of dark complexion, and have a tendency to low blood pressure, low blood sugar and relatively abnormal fatigability This predisposition perhaps depends upon a certain relation to the adrenal-sympathetic-thyroid mechanism of the organism which controls the conductivity of nerves inhibiting or stimulating the gastric cells Such cases do well under a hygienic regime with removal of the gastric irritants from the diet, antacids and adrenal nucleoprotein—H W

(ADRENIN) Respiratory metabolism in toxic glycemias (Ueber den Respiratorischen Stoffwechsel bei toxischen Glykämien) Bornstein (A) & Müller (E), Biochem Ztschr (Berl), 1921, 126, 64-76

Studies on dogs and man with pilocarpin and adrenalin, the former a stimulant of the parasympathetic, the latter of the sympathetic nervous system Pilocarpin administration is immediately followed by an increase in the respiratory quotient which must be attributed to an increased sugar oxidation Adrenalin did not produce the rise in respiratory quotient—F S H

The vascular-leucocyte formula after ADRENALIN injections (La formule vasculo-leucocytaire après injection d'adrénaline) Danul (N) & Popper (M), Ann de méd (Paris), 1921, 10, 395-399

Studies on 14 normal (?) persons The intravenous injection of 0.0005 to 0.001 mg adrenalin produces a quick hypertension lasting 3-4 minutes This is accompanied by a hyperleucocytosis in the majority of cases The leucocyte formula is variable These phenomena are believed to be purely mechanical results of arterial tension and not of specific excitation of the hematopoietic centers

—F S H

Cold abscess of the ADRENALS (*Abscès froid des capsules surrénales*) Deglos (E), Lyon méd, 1921, 130, 523-528

According to Deglos, who records an illustrative case in a woman, aged 28, rapid and complete cessation of both suprarenals with transformation of one of them into a large cold abscess is rare, especially when most of the symptoms of Addison's disease are absent Deglos' case took the form of an attenuated septicemia, with a temperature which suggested typhoid or paratyphoid fever Death took place suddenly In addition to the suprarenal lesions the autopsy showed marked hypoplasia of the ovaries and slight thyroid hypoplasia Deglos suggests that in an infective process in which several blood cultures do not explain the cause of the condition, the possibility of a cold suprarenal abscess should be considered, when very pronounced hypotension is associated with extreme prostration without the presence of other signs of chronic epinephritis —Med Sci, 5, 306

(ADRENIN, HYPOPHYSIS) The pharmacology of chelidonin, the benzylisoquinoline alkaloid of chelidonium Hanzlik (P J), J Pharmacol & Exper Ther (Balt), 1921, 18, 63-102

Cheledonin antagonizes the augmentor effects of pituitary extract on the intestine and uterus and that of epinephrin on the pregnant uterus —F A H

The influence of ADRENALIN on the white blood cell picture (*Suprareninwirkung auf das weisse Blutbild*) Hess (O), München med Wchnschr, 1921, 68, 1668

After injection of adrenalin the number of leucocytes is increased, lymphocytes often at first predominating, giving the so-called diphasic blood picture This, however, is not at all regularly observed In two cases of pernicious anaemia the behavior of the lymphocytes was identically the same two days before and after removal of the spleen —J K

Antagonistic action between atropine and ADRENALIN upon the vascular system of frogs (*Über einen Antagonismus zwischen Atropin und Adrenalin am Gefässapparat des Frosches*) Hildebrandt (F), Arch f exper Path u Pharmacol (Leipz), 1920, 86, 225-237, Ber ú d ges Physiol (Berl), 1921, 3, 340

On the Lāwen-Trendelenberg frog preparation atropine has no influence. If, however, one maintains the blood vessels in a state of constriction by long perfusion of adrenalin in concentration of 1 500,000 to 1 2,000,000 atropine may result in relaxation, proportional to the amount employed. In the splanchnic area, atropine causes constriction of the vessels, but just as in the skin-muscle area it releases the constriction caused by adrenalin although the action is weaker. On the other hand, by prolonged infusion with atropine in Ringer's solution (1 10,000 to 1 2,000) both irritability to sympathetic stimulation and to adrenalin is either lost or much diminished. Since BaCl₂ maintains its constrictor effect throughout atropine perfusion, the author believes that the inhibitory action of atropine is manifested either in the adrenalin-sensitive substance or between this and the part of the apparatus sensitive to BaCl₂.

—R G H

Technique of the extirpation of the medullary part of the ADRENALS (*Technique de l'extirpation de la partie médullaire des surrénales*) Houssay (B A) & Lewis (J T), *Compt rend Soc de biol* (Paris), 1921, 85, 1209-1210

In this article a simple method of removing the adrenal medulla and maintaining the cortex in good condition is illustrated. The directions are fairly full.—T C B

Comparative importance of the medullary and cortical parts of the ADRENALS (*Importances comparatives des parties médullaire et corticale des surrénales*) Houssay (B A) & Lewis (J T), *Compt rend Soc de biol* (Paris), 1921, 85, 1210-1212

The suprarenal medulla on the left side was extirpated in sixteen dogs, then after ten to fifteen days the right suprarenal was totally extirpated. Three dogs died within forty-eight hours of the operation. One escaped in good health and two were kept for three months in perfect health. The other ten were sacrificed for other purposes. Histological examination of the five dogs that died early or were killed showed total absence of medullary substance in four, and a minute trace in one. The authors think the three dogs that died in forty-eight hours had gross lesions of the cortex, which was the cause of death.—T C B

(ADRENALIN) Experiments on vasoconstrictor substances in the blood in high blood pressure (*Untersuchungen über gefaszverengernde Stoffe im Blute bei Hypertonien*) Hülse (W), *Zentralbl f innere Med* (Leipz), 1922, 43, 1-7

Although many believe hypertonia due to hyperadrenalinemia, Hülse was never able to confirm this. Even in cases with an enormously high blood pressure no hyperadrenalinemia nor increases in other vasoconstrictor substances were found. Some authors reg-

ularly find hyperglycemia in hypertonia, but if this were true it could not be explained as an adrenalin glycosuria. The author found that the serum of patients with Bright's disease, when injected into a normal animal, increases the sensibility of the blood vessels for adrenalin—J K

(ADRENALIN) Un caso de hipervagotonia Izquierdo (J J), Rev Mex de biol 1921, 1, 124-133

The data in somewhat abbreviated form were published in Endocrin 1921, 5, 607-609

The toxicity of the blood of ADRENALECTOMIZED frogs Kellaway (C H), J Pharmacol & Exper Therap (Balt), 1921, 18, 399-405

The adrenals were destroyed by cautery. Frogs used for testing were perfused through a sinus cannula. Of the serum to be tested, 0.2 cc was added to 2 cc of perfusion fluid. The most striking feature of the symptom complex next to paralysis of the lower limb was progressive slowing of the respiration. Neither the serum of frogs dying from decapsulation nor the serum of decapsulated frogs killed when evidently moribund "gave unequivocally positive results"—F A H

The theory of ADRENALIN formation (Zur Theorie der Adrenalin-Bildung. Erwiderung auf die Bemerkungen von K. Rosenmund und H. Dornsaft) Knoop (F), Ber d deutsch chem Gesellsch (Berl), 1920, 53, 716-718, Abst, Ber ü d ges Physiol (Berl), 1921, 4, 19

Rosenmund and Dornsaft's theory of adrenalin formation stands without biological analogy. Although it can be shown that adrenalin may be produced from tyrosin (or dioxyphenylalanin) the necessary assumption of the formation of an alcoholic hydroxyl group still remains to be overcome—R G H

(ADRENALS) Pathology of cholesterol metabolism Krontovsky (A), Pub Kiev Univ, 1918

The quantity of cholesterol in horse-serum was increased by long-continued feeding with dried brain, the amount was increased by 66 per cent after 28 days of such a diet, the internal organs did not show any modification. In another horse, which, besides this diet, was immunized by the diphtheria toxin, hypertrophy of the cortex of the suprarenals was observed as well as increase of quantity of anisotropic lipoids. Immunisation alone produced the same result—Physiol Abst, 5, 53

The ADRENALS and morphin intoxication (Les surrénales et l'intoxication par la morphine) Lewis (J T), Compt rend Soc de biol (Paris), 1921, 85, 1214-1215

It has been shown that decapsulated rats and frogs are very sensitive to morphin. The present paper deals with the results of experiments on dogs. The results are not so clear as in frogs and rats, but appear to support the idea that decapsulated dogs are more sensitive to morphin than the controls. Morphin, even in anesthetic doses, shortens the survival of decapsulated dogs.

—T C B

A clinical note on latent malaria and on the influence of ADRENALIN (*Nota clinica sulla malaria latente e sull'azione della adrenalina*) Levi (E), Gazz d osp (Milano), 1921, 42, 1185-1188

When 1-2 mgm of adrenalin is injected into a patient with latent malaria there are three possible results: (1) a typical attack of malaria with plasmodia in the blood, (2) a light attack with plasmodia, (3) a rise in temperature. If no reaction occurs the malaria is cured. A rise of temperature after the injection of adrenalin may also be seen in patients recovering from typhoid fever, erysipelas, and, sometimes, tuberculosis. The vaso-constrictor action and the increased blood pressure may stimulate the heat center.—J K

(ADRENIN) Response to drugs of excised bronchi from normal and diseased animals Macht (D I) & Ting (G C), J Pharmacol & Exper Therap (Balt), 1921, 18, 111-119

Bronchial rings or bronchial strips of the pig in Locke's solution were used. It was found that in pathological conditions there is an impairment of the normal physiological properties so that epinephrin may have little or no effect on bronchial muscle.

—F A H

(ADRENIN) A study of antispasmodic drugs on the bronchus Macht (D I) & Ting (G C), J Pharmacol & Exper Therap (Balt), 1921, 18, 373-398

Excised bronchial preparations were used. The most powerful dilators were first, papaverin and various benzyl compounds, which act on muscle cells, second, atropin, which paralyzes parasympathetic myoneural junctions, and third, epinephrin, which stimulates the sympathetic.—F A H

Is ADRENALIN a hormone (E' L'adrenalina un ormone)? Marfori (P), Gazz d osp (Milano), 1921, 42, 1096, Arch internat de pharmacod (Gand & Par), 1921, 26, 137-149, Abst Ber u d ges Physiol, 11, 109

Gley has cited evidence that the blood in the vena suprarenalis does not contain adrenalin. He stimulated the splanchnic nerve in a dog and at the same time took some blood from the suprarenal

vein This was injected into another dog, no change in blood pressure resulted Marfori believes that the quantity of blood used by Gley was too small He repeated Gley's experiments, only instead of stimulating the sympathetic he injected a small dose of adrenalin intravenously Then 30 cc of the arterial blood of the animal was injected into a second No rise of blood pressure occurred This proves that small doses may be present without being detected by Gley's method —J K

A new case of ADRENAL virilism (Un nouveau cas de virilisme cortico-surrénal) Mauclore (P), Bull Acad de méd (Par), 1920, 3 s, 84, 57-58

According to Mauclore, who records an illustrative case, Apert in 1910 collected 30 cases of suprarenal hypertrophy or tumors of the suprarenal cortex which had given rise to a masculine appearance in women Blanchard, in 1916, in a study of the pathogeny of suprarenal virilism, came to the conclusion that this condition was due to changes in the interstitial gland of the ovary, an opinion shared by Pierre Marie Symptoms of virilism may also appear at the menopause, but they are not so marked as they are in suprarenal virilism Mauclore's case was a woman aged 38, who, six years previously, had developed an abdominal tumor, and at the same time had cessation of her menses Her face, neck, and chest became covered with numerous long hairs, the face became elongated, the breasts atrophied, and the body lost its rounded form Laparotomy revealed the presence of a tumor of the right suprarenal The patient was subsequently treated with ovarian extract and her catamenia reappeared —Med Sci, 3, 218

(ADRENIN, PITUITRIN) The activity of the isolated uterus Ogata (S), J Pharmacol & Exper Therap (Balt), 1921, 18, 185-200

In the rabbit adrenalin caused an increase in tonus and in rate in the longitudinal muscle of the uterus, while the contraction of the circular muscle was increased in rate After atropin, adrenalin always produced a temporary inhibition both of circular and longitudinal muscle After ergotoxin adrenalin produced a like effect Pituitary extract often produced inhibition although usually an increase in tonus occurred in both the virgin and pregnant uterus In the rat, adrenalin caused relaxation while pituitary extract caused contraction of the uterus —F A H

Latent ADRENAL insufficiency rapidly developing after trauma
Death after surgical intervention Total destruction of the two capsules by tuberculous caseation (Insuffisance surrénale latente Evolution rapide après un traumatisme Mort subite après intervention chirurgicale Destruction totale des deux capsules par

caséification tuberculeuse) Oudard, Bull et mém Soc méd d hôp de Par, 1922, 46, 184-188

The title tells the story —F S H

Is ADRENALIN conducted along the nerves (L'adrenaline est-elle conduite le long des nerfs)? Rebello (S) & Pereira (M de M B), Compt rend Soc de biol (Paris), 1921, 85, 1163-1165

It has been maintained by Lichtwitz and denied by Meltzer that adrenalin can be conducted along nerve trunks. The authors have made eighteen experiments, employing the methods of Lichtwitz, and obtained positive results in fourteen cases. The latent period between injection and response was about 32 minutes. They conclude that the phenomena observed by Lichtwitz (cutaneous hypersecretion and dilation of the pupil) are undeniable —T C B

The mechanism of the action of ADRENALIN at a distance (Sur le mécanisme de l'action a distance de l'adrenalin) Rebello (S) & Pereira (M de M B), Compt rend Soc de biol (Paris), 1921, 85, 1166-1168

As the injection of adrenalin into a frog's hind leg attached to the body only by the sciatic nerve, gives rise to a sympathicotonic syndrome (exophthalmos, mydriasis and cutaneous hypersecretion), it is necessary to determine the mechanism of this action. The operation itself, the injection of air, the production of pain, does not cause the symptoms. Injection of adrenalin into the dorsal lymph sac, or into a normal limb always produces the symptoms in from five to ten seconds. With the sciatic nerve as the only bridge of communication between the amputated limb and the rest of the body, it was found that the injection of simple Ringer's solution gave results comparable to those obtained with adrenalin in 50 per cent of the cases. Injection of atropine causes mydriasis and augmentation of the cutaneous secretions. Eserine causes hypersecretion, and pupillary dilation. In animals that react in this way, a second injection, if that injection is adrenalin, is followed by a stronger reaction than the first. The injection of cocain, or placing a bit of cotton soaked in cocain on the sciatic, prevents the development of symptoms. The conclusion is that adrenalin is not conducted along the nerves, but the excitation is, and that adrenalin may have a specific exciting action. The long latent period is difficult to explain. It may be due to slow imbibition or slow penetration of adrenalin —T C B

Graves' disease and the ADRENAL glands (La maladie de Basedow et les capsules surrénales) Swiecicki (H), Presse méd (Par), 1921, 20, 664-665

Swiecicki, of Posen, is inclined to regard Graves' disease as due to hyperactivity of the suprarenals, the vasomotor and secretory

symptoms, including tachycardia, tremor, and exophthalmos, being caused by an increase of secreted adrenalin. He therefore recommends that treatment should aim at diminishing the production of adrenalin by administration of oil of sesame and hypotensive measures, including mild hydrotherapy, rest, and residence in a mountainous climate—*Med Sci*, 5, 301

The functional connection between the glandular portion of the OVARY and the ADRENAL cortex Serdioukov (M), Vratchebnoïé Délo (Kharkov), 1921, 2, (No 16-21) *abst Presse méd*, 1922, 30, 130

Serdioukov of the Laboratory of Experimental Pathology at the University at Saratov has carried out a series of experiments on pregnant and non-pregnant cats with a view to determining certain endocrine interrelationships. As a result of the variations in the cytological picture of interstitial cells of the ovary, the corpus luteum and the suprarenal cortex, he concludes that these glands stand in vicarious relationship with each other. This conclusion is fortified by the fact that the secretion of each tissue is of lipoid nature—R G H

(ADRENALS) The relation of melanin formation in the skin to Addison's disease (*Des mélanodermies du type Addisonien*) Sézary (A), *Presse méd (Par)*, 1921, 29, 281-283

Sézary remarks that the sympathetic system has long been regarded as responsible for the pigmentation found in Addison's disease, but he can find no adequate evidence for this hypothesis. On the other hand, he marshals many facts which tend to show that this pigmentation is due to an increase of the normal melanin-forming function of the skin and that this increased function is brought about by various endocrine disorders. He does not suggest that any one of the endocrine glands is alone to blame—*Med Sci*, 5, 306

Total ADRENAL insufficiency Asthenia and intoxication (*Insuficiencia adrenalínica total Astenia e intoxicación*) Soler (F L), *Semana méd (Buenos Aires)*, 1921, 28, 361

Dogs under chloral-morphine anesthesia died within 13 hours after bilateral extirpation of the two suprarenal glands. Their cerebral motor zone was not irritable and they gave a practical demonstration of the final conclusion of Cheyne-Stokes syndrome. Soler concludes that capsular insufficiency produces death by facilitating morphine poisoning—B A H

(ADRENIN) The sensitiveness to poisons in avitaminous animals Van Leeuwen (W S) & Verzar (F), *J Pharmacol & Exper Therap (Balt)*, 1921, 18, 293-311

Among other things the blood pressure reaction to adrenalin of normal and avitaminous fowls and cats was studied. The reaction did not differ materially in the two cases. It was concluded that the decreased activity of smooth musculature in avitaminosis is probably caused by a lack in the body of these animals of the normal chemical agents—F A H

Paradoxical behavior of sugar metabolism on the simultaneous administration of pilocarpin and ADRENALIN ("dissimilatory conversion") [Ueber ein paradoxes Verhalten des Zuckestoffwechsels bei gleichzeitiger Einwirkung von Pilocarpin und Adrenalin ("Dissimilatorische Umkehr")] Vogel (R) & Bornstein (A), Biochem Ztschr (Berl), 1921, 126, 56-63

Although both adrenalin and pilocarpin, when given separately, induce hyperglycemia, when they are administered simultaneously there results at first slight hypoglycemia, which is later followed by a rise in blood sugar. This is interpreted as indicating that the pilocarpin hyperglycemia mechanism differs from that of adrenalin hyperglycemia—F S H

BLOOD SUGAR metabolism (Blutzuckerstoffwechsel) Meyer (E), Berl klin Wchnschr, 1921, 58, 1542-1543

When normal individuals, patients with epilepsy, dementia paralytica, icterus, or encephalitis take 20 grams of glucose on an empty stomach they show a rise of the blood sugar with its maximum in the second half hour after the injection. When, later, 100 grams of glucose is given the blood sugar rises only in icterus and in nitrobenzol intoxication. In diabetes the rise of the blood sugar after 20 grams of glucose is much more intense. The regulation of the blood sugar depends upon the liver, the pancreas, the bowels, the central nervous system and the endocrine organs—J K

The BLOOD SUGAR in surgical diseases (Das Verhalten des Blutzuckers bei chirurgischen Erkrankungen) Seitz (E), Mitt a d Grenzgeb d Med u Chir (Jena), 1922, 34, 514-526

Some time ago the author published in Arch f klin Chir, Vol 112, observations to the effect that in patients who have a high alimentary hyperglycemia without diabetes, infections with staphylococci are extremely frequent. He now has examined other diseases. He found that in tuberculosis, also, there is very often a marked alimentary hyperglycemia. This is not due to cachexia, since it is not found in cancer. The blood sugar was studied in cases of Graves' disease also, and the alimentary hyperglycemia was found to be high. This is probably due to the increased irritability of the sympathetic system. It was found that 14 days after an operation for Graves' disease the sugar metabolism and the tonus of the involuntary nervous system had become normal. It

is remarkable that in some cases of diffuse colloid goiter after strumectomy alimentary hyperglycemia and the sympathetic tonus were increased Seltz believes that Graves' is a primary thyroid disease If this were not true, it would be difficult to explain why sugar metabolism becomes normal almost immediately after strumectomy The rapid restoration of carbohydrate equilibrium shows also the excellent results of surgical treatment in Graves' disease
—J K

CHOLIN as a peristaltic hormone (*Cholin als Hormone der Darmbewegung*) Magnus (R), *Naturwissenschaften*, (Berl), 1920, 8, 383-388

After a general account of intestinal movement, the author goes on to allude to the work of le Heux, who regards choline on experimental evidence as the main chemical stimulus of Auerbach's plexus, and fully endorses this view The origin of choline is the lecithin of protoplasmic cells, its activity is controlled by some antagonistic substance with the same action as atropine, and may be intensified by the formation of certain esters as in acetylation (Dale, Reid Hunt) If this occurs in the intestine the presence of synthetic enzymes capable of forming choline esters is postulated It is possible that choline may play a similar rôle in other organs
—*Physiol Abst*, 5, 415

The influence of Karlsbad water and salt on DIABETES, and a new theory on this disease (*Die Wirkung des Karlsbader Wassers und Salzes auf Zuckerkrankte, beurteilt nach einer neuen Auffassung über den Diabetes*) Arnoldi (W) & Roubitschek (R), *Deutsche med Wchnschr* (Berl), 1922, 48, 250-251

The authors introduce a new theory on diabetes They believe that it is caused by a disturbed transport of the sugar through the body The cells are less permeable for glucose on account of a change in the protoplasm The protoplasm is probably changed by an abnormal proportion between K, Na, Ca, etc, ions The excellent results procured by the use of Karlsbad water may be due to a restoration of the normal proportion of metallic ions Ordinary water, when ingested by a normal person, has no influence on the blood sugar, when Karlsbad water is given the blood sugar sometimes sinks, sometimes is not affected In the majority of cases of diabetes the blood sugar sinks, sometimes even very markedly, after the ingestion of Karlsbad water —J K

DIABETIC retinitis (*Rétinite diabétique*) Chauffard (A), *J des Praticiens* (Par), 1922, 36,—(No 3), *Abst Presse méd* (Par), 1922, 30, 155

The case is described of a woman of 78 who had had visual troubles for two years There was also latent or slight glycosuria

and glycemia of 3 gm , but with good general health and no other diabetic signs except that the ophthalmoscope showed retinitis similar to that of albuminuria or nephritis There was, however, no albuminuria nor increased blood nitrogen Such findings are characteristic also of retinitis of pregnancy The author explains the common retinoscopic picture in each of these conditions as due to a concomitant cholestrinemia He assumes that the excessive amount of circulating cholesterol leads to its deposit in the inflammatory exudates —R' G H

Curve of sugar excretion in severe DIABETES Felsher (H), J Biol Chem (Balt), 1922, 50, 121-129

"The work reported in this paper represents a study of the total quantities of sugar excreted in a number of diabetic patients during periods in which they were being held in the non-diabetic status by dietary restriction, and during the periods in which the diets were gradually increased until clearly abnormal quantities of sugar appeared in the urine " "Study of the curves obtained lead to the conclusion that individuals with severe diabetes, when brought into the non-diabetic status, by fasting or other more suitable adjustments of the diet, may then excrete small quantities of sugar not greater than those excreted by normal individuals under parallel conditions The quantities in the series averaged 10 and 15 mg per kilo per day As the diet is gradually increased step-wise at 1 to 4-day intervals there is at first little or no permanent increase of the sugar excretion " When the total glucose equivalent of the diet has risen above a certain limit (which varies with the individual), however, further additions to the diet lead to sudden and rapid accelerations of sugar excretion out of proportion to the preceding output This observation is in harmony with the well known conception of a clearly definable "tolerance limit" for glucose in diabetes —F S H

Modern theories and treatment of DIABETES (Die moderne Entwicklung der Theorie und der Therapie des Diabetes mellitus) Frank (E), Wien klin Wchnschr , 1921, 35, 70-71

This article is a good, brief, up-to-date general review, without new data —J K

Pancreatic DIABETES in dogs deprived of the ADRENAL medulla (Diabète pancréatique chez les chiens privés de la partie médullaire des surrénales) Houssay (B A) & Lewis (J T), Compt rend Soc de biol (Paris), 1921, 85, 1212-1213

Five dogs were operated upon The medulla of the left suprarenal was extirpated, then the right suprarenal gland About one month later the entire pancreas was removed Two dogs survived one eight days and one three days Both had hyperglycemia and

glycosuria Histologically there was complete absence of medullary substance in one case, and a minute fragment in the other (eight days of diabetes with the strongest glycosuria) The other three presented no variation in glycemia One did not eat and died of peritonitis four days after pancreatectomy The other two died six and twenty-four hours after a difficult pancreatectomy

—T C B

Secondary DIABETES in pigmentary cirrhosis (*Le diabète secondaire dans la cirrhose pigmentaire*) Lereboullet (P) & Mouzon (J), *Bull et mém Soc méd d hôp de Par*, 1922, 45, 1681-1689

The important point in this case report is the tardy appearance of diabetes some four years after the onset of pigmentation and hepatomegaly —F S H

Organotherapy in DIABETES (*Ueber Organotherapie bei Diabetes mellitus*) Loening (K) & Vahlen (E), *Deutsche med Wchnschr (Berl)*, 1922, 48, 217-219

Vahlen has prepared a substance from the pancreas of a cow, which he calls metabolin There is a substance in yeast differing only slightly from metabolin Administration of this substance to diabetics has one of three effects (1) Absolutely no result, (2) incomplete result, the sugar in the urine being diminished, (3) complete result, the sugar disappearing Some case reports are given The authors fail to tell the preparation of the substances used and do not give the quantity of blood sugar, which is much more significant than urine sugar —J K

A study of the Wassermann reaction in 140 cases of DIABETES mellitus Rosenbloom (J), *Proc Soc Exper Biol & Med (N Y)*, 1921, 18, 236

In a study of 140 cases of diabetes mellitus, a positive Wassermann reaction was found in sixteen cases Eight of these presented signs of tertiary syphilis These eight were treated for the existing syphilis There was no increase in tolerance for carbohydrate following the treatment This may be due to the fact that the fibrosis of the pancreas produced by the syphilis is not changed by the treatment —R G H

Blood pressure studies in 140 cases of DIABETES mellitus Rosenbloom (J), *Proc Soc Exper Biol & Med (N Y)*, 1921, 18, 236-237

Blood pressure estimations were carried out on 140 cases of diabetes for varying lengths of time Some have been studied for as long as ten years It appears that the blood pressure in un-

complicated diabetes is normal or slightly under normal In every case of elevated blood pressure in this series were found complications such as aortitis, arteriosclerosis, nephritis, cardiac hypertrophy and aortic endocarditis In conditions of acidosis the blood pressure falls The presence or absence of hyperglycemia had no effect on the blood pressure—R G H

Treatment of DIABETES (Behandlung des Diabetes) Schreiber (E), Berl klin Wchnschr, 1921, 58, 1543

Not too much protein and much fat is the best diet in diabetes The "Mehlfruchtekur" of Falta may be recommended No novel data are offered—J K

Relation between DIABETES and syphilis (Contribution a l'étude des rapports du diabète et de la syphilis Un cas de diabète sucré apparu quelques jours après un chancre syphilitique) Vallaret (M) & Blum (P), Bull et mém Soc méd d hôp de Par, 1922, 46, 90-94

Report of a patient who developed diabetes a few days after chancre The patient had not been previously diabetic Diabetes developed side by side with the syphilis—F S H

DIABETES INSIPIDUS Anon, Med Sci (Lond), 1922, 5, 396-401

An interesting review of some of the more important recent literature—R G H

(DIABETES INSIPIDUS) The rhythm of hypophysary polyuria Bergé (A) & Schulmann (E), Med Press & Circ (Lond), 1921, 1, 454-456

Bergé and Schulmann summarize the characteristics of the polyuria in diabetes insipidus as follows (1) The quantity eliminated is variable, no approximate figure being assignable, (2) The polyuria is more pronounced at night, (3) The quantity of urine excreted is at times greater than that of the fluid ingested (dehydration), (4) There are no notable modifications of the excretion attributable to variations of régime, (5) There is no important disturbance of the chemical composition of the urine, generally speaking there is a slowing of metabolism and a tendency to demineralization, the amount of uric acid is small, there is no glycuronic disturbance, (6) Absolute renal integrity has been verified by (a) elimination of methylene blue, (b) persistence of the faculty of ureal concentration and maintenance of normal quantity, (7) Controlling action of extract of the posterior lobe of the hypophysis on the polyuria—Med Sci, 5, 398

DIABETES INSIPIDUS complicated by intermittent glycosuria Evans (G) & Wallis (R L M), Lancet (Lond), 1921, 1, 70-72

Evans and Wallis record two cases of diabetes insipidus complicated by glycosuria, the intermittent nature of which distinguished them from the cases of diabetes innocens described by Salomon. The writers regard the cases as examples of a pituitary dystrophy comparable to those cases of thyroid dystrophy in which there is no marked change in the size of the gland and no distinct clinical picture of either hypo- or hyper-function—*Med Sci*, 5, 398

Gastro-intestinal conditions in DIABETES INSIPIDUS (*Über das Verhalten der magen-und Darmfunktion beim Diabetes insipidus*)
Gorke (H) & Deloch (E), *Med Klin* (Berl), 1921, 17, 1140-1142

Gorke and Deloch, of the Breslau University Medical Clinic, report three cases of diabetes insipidus in which, in addition to polyuria, polydipsia, anhydrosis, and increase in molecular concentration of the blood, the following gastro-intestinal symptoms were found, viz Hyperacidity, hypersecretion, increased gastric peristalsis and spastic constipation of the large intestine. The writers regard these disturbances of gastro-intestinal function as connected with the lability of the vegetative nervous system present in these cases, and attribute the favorable effect of pitu-glandol on the symptoms either to its direct action or to indirect action by the agency of the vegetative nervous system—*Med Sci*, 5, 399

Treatment of DIABETES INSIPIDUS with PITUITRIN and pitu-glandol (*Diabète insipide traité par la pituitrine et le pituglandol*)
Urechia (C I) & Alexandrescu-Dersca (C), *Bull et mém Soc méd d hôp de Par*, 1922, 46, 190-195

Report of one case, female, aged 35 years. The polyuria was alleviated by injections of pituitary preparations. The diminution was in general proportional to the size of the dose—*F S H*

Diseases of the DUCTLESS GLANDS Rolleston (J D) & "G W,"
Med Sci, 1922, 5, 300-313 }

A review of recent literature, several paragraphs of which are reproduced as abstracts in this number of *Endocrinology*
—R G H

An ENDOCRINAL factor in general paresis Davis (T K), *Am J M Sc* (Philadelphia), 1922, 163, 425-430

Based upon the ideas that status lymphaticus can be used as an indication of hypoplasia of adrenal cortex and that trichosis in an individual can be used as a measure of suprarenal valence, the author reports upon 82 cases of general paresis which he has thus examined. His conclusions are (1) The endocrinal status of the individual has a discernible influence in determining whether, once

infected with syphilis, he is likely to develop paresis, (2) status lymphaticus is rare among male paretics and is seen less frequently among paretics than among male hospital cases which come to autopsy, (3) individuals who have low suprarenal functioning appear to develop paresis less frequently than strong suprarenal individuals, (4) the course of general paresis on the average varies in rapidity directly with the suprarenal strength of the individual

—J F

ENDOCRINE status and dynamism of gastro-crino-kinetic drugs

Duran (F), Arch di farmacol sper (Roma), 1921, 31, 135-142, 177-183

Atropine diminishes the acidity and the digestive power of the gastric juice, while pilocarpine has the opposite effect. The endocrine preparations, thyroglandol, pitnoglandol, adrenalin and pancreatin, increase the acidity without affecting the digestive power. Suprarenal preparations do not counteract the effect of either atropine or pilocarpine in these respects, while thyroid and pancreatic preparations inhibit both the decreased motility caused by atropine and the increased motility caused by cascara —Chem Abst, 16, 439

Neurasthenia as ENDOCRINE syndrome (La neurasthénie considérée comme un syndrome endocrine) Goormaghtigh (N), Arch méd belges (Brux), 1921, 74, 1040-1045

The article is an abbreviated translation of a recent article by Harrower —R G H

Constitution and the ENDOCRINE system (Konstitution und endokrines System) Hart (C), Ztschr f ang Anat [etc], (Berl), 1920, 6, 71-84

A general article calling attention to the specific endocrine pattern of every individual whereby growth, development, form, psychic function and other manifestations of life are determined. Pathological conditions particularly mentioned as endocrinopathies are status thymo-lymphaticus, infantilism, eunuchoidism and mongolism. While status thymo-lymphaticus and infantilism may be inherited, the same symptoms may result from intra- or extra-uterine disturbances of the endocrine organs so that it is difficult to decide whether in a given case it is inherited or acquired. The author warns against the association of such anomalies with a particular ductless gland and believes it erroneous to explain infantilism as being due to hypofunction or disfunction of the thyroid. He also objects to classifying infantilism as dysgenitalism, maintaining that there is always a general involvement of the whole endocrine system. Regardless of the primary cause, or the particular ductless gland which is most affected, general involvement

of the endocrine system must also be recognized in the other three abnormalities mentioned above and possibly also in asthenia universalis Just as the normal so the pathological pattern is under endocrine dominance No bibliography—A T R

(ENDOCRINE GLANDS) Glandular dystrophies and particularly mono-symptomatic dystrophies (*Dystrophies glandulaires et particulièrement dystrophies mono-symptomatiques*) Hutinel (V) & Maillet (M), *Ann de méd* (Paris), 1921, **10**, 364-385

A continuation of the discussion previously reported—F S H

(ENDOCRINE ORGANS) Atrophy of human organs in inanition (*Über die Atrophie der menschlichen Organe bei Inanition*) Krieger (Maile), *Ztschr f ang Anat* [etc], (Berl), 1920, **7**, 87-134

The organ weights are given in 135 cases (in six groups as follows I, 11 cases without chronic disease, II, 7 with chronic dysentery, III, 27 with malignant tumors, IV, 31 with chronic general infection, V, 40 with tuberculosis, VI, 19 various cases of senility) where the body had lost from 35.8 to 48.4 (average of each group) The spleen showed a loss of 46.6 per cent in group I, 36 per cent in group II, 27.6 per cent in group III, and 48 per cent in group VI The pancreas showed a loss of 44.8 per cent in group II, 33 per cent in group III, 30.5 per cent in group IV, and 28.6 per cent in group V The thyroid showed a loss of 47 per cent in group II, 20.6 per cent in group III, 32.3 per cent in group IV, and 35.8 per cent in group V The suprarenals together showed a gain in weight in nearly all cases, the figures for the four groups where weights were taken being Loss of 8.6 per cent (from his figures and not 17.2 as tabulated) in group II, gain of 21.5 per cent in group III, gain of 23.2 per cent in group IV, and a gain of 6.6 per cent in group V The testes showed a loss of 41.3 per cent in group II, 28.7 per cent loss in group III, 40.3 per cent loss in group IV, and 49.4 per cent in group V The hypophysis showed practically no change in weight although only 30 glands were weighed and these belonged to groups II, III, IV and V Similar tables are given for the liver, heart, kidney and brain These results are compared with the observations others have made on the cat, dog and pigeon Eighteen cases are given in detail Some references are given

—A T R

The interrelations of the ENDOCRINE ORGANS in Graves' disease, in diabetes and the rejuvenation problem (*Die Wechselwirkungen der Blutdrüsen bei der Basedow'schen Krankheit, dem Diabetes mellitus und dem Verjüngungsproblem*) Leschke (E), *Wien med Wehnschr* (Wien), 1921, **71**, 27-33

According to Leschke, growing old, at least in the human subject, is caused not only by extinction of the function of the interstitial generative glands, but in a still greater degree by suppression of the function of the other glands of internal secretion, among which the anterior lobe of the hypophysis and the suprarenal cortex play the most important part. In attempting to produce an artificial rejuvenation in man Leschke endeavors to stimulate the suprarenals, thyroid, and hypophysis by x-rays, and does not confine himself to stimulating the generative glands by ligature of the vas deferens, irradiation of the testes or ovaries, or transplantation of portions of these organs. In the estimation of the results of supposed rejuvenation, Leschke recommends the exercise of considerable reserve, especially as one has to depend on the statements of patients who may have been influenced by the propaganda in the daily press —Med Sci, 5, 310

Glandes ENDOCRINES et syphilis fonctionnelle ou meliopragique
Merklen (P), La Médecine (Par), 1921, 2, 774-776

In a general discussion Merklen points out that syphilis may play a significant etiologic role in the pluriglandular endocrinopathies. Antiluetic treatment in such cases is important —R G H

(ENDOCRINE ORGANS) Etiology of post-war late rachitis (Spätrachitis in der Nachkriegszeit und Konstitution. Ein Beitrag zur Ätiologie der Erkrankung) Neuberger (H), Ztschr, f ang Anat [etc] (Berl), 1921, 8, 15-41

From an analysis of 38 (33 male and 5 female) patients from 12 to 20 years of age, it is concluded that disturbances of one or more ductless glands (gonads, thyroid, parathyroids, thymus, hypophysis, and perhaps also the pineal gland and suprarenals) are nearly always present in calcium deficiency diseases of the bones, such as rickets and osteomalacia, the proper functioning of the endocrine system being apparently necessary to normal calcium and phosphorus metabolism. Lack of vitamins may be a primary factor in producing this glandular disfunction. A short list of German references is given —A T R

The relations between the ENDOCRINE ORGANS and abnormalities of teeth and jaws (Die endokrinen Drüsen in ihrer Beziehung zu Zahn und Kieferanomalien) Petzel (W), Deutsche med Wchnschr (Berl), 1922, 48, 231

A good short review of the literature. No new data are added —J K

Asthenias of ENDOCRINE origin (Le diagnostic des asthenies d'origine endocrinienne) Sézary (A), Presse méd (Par), 1922, 30, 79-81

Sézary recalls that asthenia is common to innumerable diseases of totally different origin, and points out that an unfortunate tendency to blame the endocrine glands for every symptom is becoming prevalent. Although asthenia is doubtless the most frequent symptom of endocrine disturbances, and characteristic of Addison's disease in which histologic examination rarely fails to reveal *adrenal* lesions, anatomical findings do not support the conclusion that the asthenia of every endocrine syndrome is merely caused by adrenal insufficiency. Sézary recognizes two distinct types of asthenia which are both of endocrine origin. The first type is connected with adrenal lesions and combined with muscular weakness and extreme fatigability; it occurs in Addison's disease and in epinephrectomized animals, myasthenia would be the better term, as the muscle itself becomes exhausted and the symptoms correspond with the disease of that name (Erb and Goldflam's myasthenia). The second type does not furnish evidence of adrenal involvement at necropsy, although asthenia is present, and there is no increased muscular fatigability. These types can be distinguished by means of the dynamometer: the rapid muscular exhaustion of adrenal insufficiency gives a curve with sudden drop, the muscular weakness of other asthenic conditions shows a slowly declining curve, similar to that of muscular fatigue in normal persons. The test is of therapeutic value, for improvement can be obtained by administration of total adrenal substance when adrenal involvement is actually present, whereas little benefit results when the adrenals are not at fault. In the case of a woman confined to her bed for ten years by muscular weakness, such as to prevent her from standing for more than ten minutes at the time (a case of *adiposis dolorosa*) the dynamometer showed a gradual decline, suprarenal therapy caused but a slight, transient improvement, but **thyroid** medication accomplished a complete cure. In a case of tuberculous meloderma, with pigmentation even of the mucous membrane, the dynamometer did not register the sudden drop of muscular fatigability and necropsy revealed marked degeneration of the liver with intact adrenals. Erb and Goldflam's bulbar asthenia, is characterized by weakness of the oculomotor, facial and cervical muscles, followed by paralysis with demonstrable inflammatory lesions in the muscles; asthenia of adrenal origin does not show any predilection for the muscles enervated by cranial nerves and is not followed by paralysis. These examples show that not all myasthenias even are referable to adrenal insufficiency; they are presented with the object of furthering a more accurate classification of asthenic conditions of endocrine origin. Sézary states that he found adrenal lesions at necropsy in every case in which rapid muscular fatigability had been observed, he questions the existence of adrenal insufficiency when histologic examination fails

to reveal caseous degeneration, invading tumors, extensive necrosis or sclerosis of the adrenal glands—G L

(GONADS) *Hermaphroditismus spurius masculinus* Frohlich, Berl klin Wchnschr, 1921, 58, 1544

The patient was a man of 18 with a complete male habitus but without erections or pollutions. The distribution of hair was completely male. The external sexual organs were very small, there was a hypospadias perineoscrotalis. Prostate and seminal vesicles could not be found. As a tumor was felt in the abdomen a laparotomy was carried out. The left sexual gland was enlarged and contained testicle as well as tumor tissue (epithelioma chorioectodermale). The right gland was replaced by an enormous tumor. It was attached to a ligamentum latum. On the right side a fallopian tube with fimbriae was found. There was no uterus.

—J K

(GONADS, BIDDER'S ORGAN) Investigation of Bidder's organ of male and female toads (*Untersuchungen über das Biddersche Organ der männlichen und weiblichen Krotten. I. Mitteilung. Die Morphologie des Bidderschen Organes*) Harms (W), Ztschr f Anat u Entwicklungsgesch, (Berlin), 1921, 62, 1-38

The article deals with the general history, development and significance of Bidder's organs with special reference to the secondary sex characters, and the interstitial cells of the testis and ovary of the toad. In *Bufo vulgaris* the annual cycle of the ovary, testis and Bidder's organ in relation to the breeding habits is given in detail. In the male, Bidder's organ decreases one-half or even two-thirds of its original volume during and for two months after the breeding season, while in the female this organ acts just the reverse by increasing enormously during and for some time subsequent to the breeding season. The author maintains that the interstitial cells of the testis (which he regards as merely storage or transporting organs for products of the sex cells proper) the lutein cells of the ovary and the granulosa cells of Bidder's organ discharge their inclusions into the blood stream and thus affect the secondary sex characters. Animals with only Bidder's organ intact (concerning which he promises a second "Mitteilung"), the testes having been removed, show the usual secondary sex characteristics during the breeding season. Both gross and microscopic illustrations of the organ are included. An extensive list of references is given.—A T R

(GONADS) *Hermaphroditismus externus* without internal genital organs. Holst (J) Norsk Mag f Laegevidensk (Kristiania) 1921 82, 177-181

Holst reports one case. A person 21 years old who passed as a woman. She was well educated and intelligent, but did not know to what sex she belonged. She entered the hospital because of a large tumor in her lower abdomen. The external genitalia consisted of a penis or clitoris 4 cm long, at the base of which was the urethral opening so situated as to form a pronounced hypospadias. Posterior to the "penis" were two skin folds simulating the labia majora. The labia minora were absent. About 2 cm below the urethral orifice was the opening of a 5 cm canal, the lumen of which admitted the point of a pencil. This extended upwards and backwards to end blindly near the rectum. There was no evidence of either scrotum or testicles and the inguinal canals were empty. The tumor, removed by operation, was about the size of a man's head. It filled the true pelvis and was attached by two broad pedicles to the region of the ovaries. Symmetrically placed on the tumor were two structures that looked somewhat similar to Fallopian tubes, microscopically they also resembled tubes. A most careful macroscopic and microscopic examination failed to reveal any other sign of internal genital organs. The patient recovered from the operation. The first microscopic diagnosis made was adenocarcinoma from ovarian epithelium, but Holst is inclined to consider the new growth a teratoma containing only one type of tumor tissue.

As to secondary sexual characteristics. The voice had the timber of an adolescent male, there was some beard present, and the mammary glands were too small for a female and too large for a male.—D J G

Morphology of the female GONADS in the domestic animals (Beitrag zur Morphologie der weiblichen Geschlechtsorgane bei den Säugetieren). Kùpfer (M), Vrtijschr d naturf Gesellsch in Zurich, 1920, 65, 377-433, Abst, Schweiz med Wehnschr (Basel), 1921, 51, 984

In a great mass of material Kupfer studied the evolution of the corpus luteum. Both evolution and devolution were found to be regular. At each ovulation there developed from the ruptured follicle a corpus luteum, which, after it had reached its full development, retrogressed. An intervolution period was thereby delimited which, in cows, lasted 31 days. In the intervolution period the evolution of the corpus luteum took place, while at the same time a new Graafian follicle developed. The intervolution period was ordinarily related to ovulation but did not regularly synchronize with the rutting period. Ovulation was apparently not determined in any way by copulation. Uterine hemorrhage which did not invariably occur was likewise not definitely related to rutting and ovulation.—R G H

(GONADS) Specific actions of sex hormones and embryonal asexuality (L'action spécifique de la sécrétion interne des glandes sexuelles et l'hypothèse de l'asexualité de la forme embryonnaire) Lipschütz (A), Rev Scient (Par), 1921, — — (No 1), Reprint 15 p

The author emphasizes the fact that though interstitial cells may be absent in batrachians and birds, they constitute a well marked endocrin gland in mammals. Whatever may be said as to the intrinsic sexuality of the fertilized ovum, the gonadal hormones play an important rôle in the efflorescence of the sexual characteristics. The paper, being itself largely a summary, should be consulted for details in the original — R G H

(GONADS) Eunuchoidism in the rabbit, with the presence of spermatozoa in the canaliculi and with defective interstitial cells (Ueber Eunuchoidismus beim Kaninchen in Gegenwart von Spermatozoen in den Hodenkanälchen und unterentwickelten Zwischenzellen) Lipschutz (A), Bormann (T) & Wagner (K), Deutsche med Wchnschr (Berl & Leipz), 1922, 48, 320-322

The authors observed a rabbit with eunuchoid habitus, many spermatozoa in the testicles and poorly developed interstitial cells. The penis was very small. In a second animal of the same litter puberty was retarded, spermatozoa were also present, but the interstitial cells were small. Therefore, the authors agree with Steinach that the interstitial cells are the puberty glands, and that the seminal cells have no influence on the secondary sexual characteristics — J K

(GONADS) Dysgenitalism in two brothers (Dysgenitalismus bei zwei Brüdern) Mayer (C), Wien klin Wchnschr 1922, 35, 118

Two brothers of 26 and 24 years, respectively, showed a typical eunuchoid habitus. Each had the penis and testicles of a small child, no beard, no axillary hairs and a sella turcica of normal size. Only the elder brother had pubic hair. Both were very intelligent, both had enlarged tonsils. One of them had a small goiter — J K

(GONADS) The psychopathology of puberty and adolescence. The Morison Lectures for 1921. Mott (F), J Ment Sc (Lond), 1921. The second Maudsley Lecture, 1921. Mott (F), J Ment Sc (Lond), 1921.

In these four lectures are included among much varied and interesting material the results of Mott's prolonged and original observations on the morbid lesions in the testis and ovary in both germinal and acquired mental disease. The present abstract refers

to this work alone. In dementia praecox, Mott finds that the testis undergoes regressive atrophy, which, according to the duration of the disease, varies from the slightest morphological and biochemical changes to total atrophy of the seminiferous tubules and cessation of spermatogenesis. Speaking generally, he finds that the earlier the onset of symptoms and the longer the duration of life subsequently, the more complete the atrophy. Even the testis of a man of 80 years showed much clearer signs of functional activity. On the other hand, in such an acquired form of mental disease as dementia paralytica, the atrophic changes are focal, and side by side by areas of ovary from cases of dementia praecox shows changes of the same order. To the naked eye the organ is smaller and lighter than normal and has a crinkled appearance. This is true even when the patient has had a child, and such patients appear rarely to have more than one. Microscopically, there is no evidence of recently matured Graafian follicles. The continuous zone of primordial follicles normally found in early life is absent in this disease. Such small follicles as are present show evidence of degeneration. Such regressive atrophy is not found in dementia paralytica. The critical periods of life as regards mental disease, Mott believes to be adolescence and the climacteric, that is, when the sexual function becomes mature and wanes, respectively. He believes this to indicate important relations between sexual functions and mental disease. Discussing the question whether the atrophy of the sexual organs is the cause or an accompaniment of the mental symptoms he concludes that there is a germinal-biochemical failure of all nuclear material in the body, but of that of the central nervous system and sexual organs particularly, with a corresponding defect of reproductive and "psycho-physical" energy. This failure in many cases begins before puberty. Turning then to the essential lesion of the nervous system in dementia praecox, Mott concludes, from his own observations and those of Nissl, Alzheimer, and others, that this consists in a parenchymatous degeneration of the neurones with relatively little morbid change in the mesodermic supporting tissues. The histological peculiarities of the affected neurones are described at length, and Mott concludes that a failure of oxidation processes dependent upon a defect of the vital energy of the nucleus underlies the mental manifestations. A similar failure accounts for the regressive changes seen in the sexual organs. An admirable series of drawings illustrated the series of lectures—Med Sci, 5 332-333

(GONADS) Castration of hen-feathered Campines. Morgan (T. H.)
Proc Soc Exper Biol & Med (N. Y.), 1920, 17, 70

See Endocrinology 4, 381-355

(GONADS) Vasectomy practiced on a dog with a view to rejuvenation (*Vasectomie pratiquée chez un chien dans un but de régénération*) Sand (K), *Compt rend Soc de biol (Paris)*, 1921, 85, 1201-1205

The author gives a full description of the results of a bilateral vasectomy on a decrepid dog, over twelve years of age, done with the aim of rejuvenating the animal. The operation, a vasectomy on the left side, a resection of the epididymis on the right, was done May 23, 1921. After a few weeks the dog began to improve. Nutrition was nearly normal, the force and tonus of the muscles was satisfactory. He preceded a bicycle going at a rate of 15 km per hour. The skin was supple, and the hair was smooth and shiny. He walked with a free gait and held his head high. He again showed interest in the female and had coitus on November 20th. The animal seemed full of life.—T C B

(GONADS) Internal secretion and especially Steinach's rejuvenation (*Ueber innere Sekretion, speziell über die Steinachschen Verjüngungsversuche*) Schmidtgen & Gruber, *Berl klin Wchnschr*, 1921, 58, 1547-1548

Steinach's rejuvenation is not a real rejuvenation but only a return of sexual desires. Though the experiments of Steinach are highly interesting there has been as yet no justification established for carrying out his operation in man. It has not been proved that an animal lives longer after Steinach's operation than it would have done without it.—J K

Development, structure and significance of the interstitial cells of the GONADS (*Entwicklung, Bau und Bedeutung der Keimdrusenzwischenzellen*) Stieve (H), *Ergebn d Anat u Entwicklungsgesch (Wiesb)*, 1921, 23, 1-249

An extensive and critical review of the literature with special reference to the endocrine function of the ovary and testis. Nearly 1,000 references are listed. No new data are added.—A T R

(GONADS) The effects of ligation of the vas deferens (*Over gevolgen van vas deferens onderbinding*) de Vrieze (T J), *Nederl Tijdschr v Geneesk (Haarlem)*, 1922, 66 (I), 266-281

A man of 63 suffered from vomiting, constipation and want of appetite. He also had hypertrophy of the prostate. The patient was energetic and vigorous. A ligation of both vasa deferentia was made because of the hypertrophy of the prostate. After this the patient became extremely quiet, did not leave his bed any more, had no appetite at all, had no interest in anything. He died of cachexia. Autopsy showed hypertrophy of the prostate, cystitis and purulent

pyelonephritis The testicles were atrophic without spermatogenesis There was no increase in the number of interstitial cells This is the first case of this operation with a report of a post-mortem examination —J K

Diabetes insipidus and HYPOPHYSEAL INFANTILISM (*Diabete insipido ed infantilismo di origine ipofisaria*) Antonelli (G), Policlin (Roma), 1920, 27, 1203-1210, Sez Prat

According to Antonelli, who records an illustrative case, Strauss in 1912 was the first to draw attention to the relation between diabetes insipidus and arrest of development, and cases of this kind have since been reported by Ebstein, Kopezynski, Lereboullet, Faure-Beaulieu and Vaucher, and Souques and Chauvet In Antonelli's case, which occurred in a man aged 23, in whom arrest of development occurred at 13, pituitary involvement was shown by intense polyuria, attacks of headache and giddiness, asthenia, optic atrophy, bitemporal hemianopsia, low blood-pressure, and somnolence In the absence of an autopsy the nature of the pituitary lesion could not be determined, but in view of the long history it was probably a benign tumour —Med Sci, 5, 398-399

Autoplastic transplants of the epithelial HYPOPHYSIS in larvae of *Rana pipiens* Atwell (W), Anat Record (Phila), 1922, 23, 8

The epithelial hypophysis was transplanted from the head to the tail in very young tadpoles The experimental animals failed to develop the typical silvery appearance of the hypophysectomized tadpole They were, however, lighter in color than normal larvae Examination of the living tadpole under the binocular microscope showed that the melanophores were not so contracted nor the xantholeucophores so widely expanded as in the typical silvery larva The hypophysis, or at least the pars intermedia—which is responsible for the color change—had been only partly compensated for by the transplant The condition is evidently that of a chronic hypophyseal insufficiency —Author's abst

(HYPOPHYSIS) Obesity in essential hydrocephalus (*L'obésité dans l'hydrocephalie essentielle*) Babonneix (L) & Denoyelle (L), Bull et mém Soc méd d hôp de Par, 1922, 46, 150-158

A case report and review of the literature, the conclusion of which is that essential hydrocephalus can be complicated by obesity in certain cases This obesity seems to be produced by an interesting lesion, not of the hypophysis, but of the infundibulum or the epiphysis —F S H

Radium treatment of HYPOPHYSEAL tumor in acromegalic syndrome (*Radiumterapia dei tumori ipofisari a síndrome acromegalica*) Bertolotti (M), Gior d r Accad di med di Torino, 1920, 83, 110-122

Bertoioiti records the case of a man, aged 35, who was admitted to hospital with all the signs of a rapid and malignant attack of acromegaly, viz., almost complete blindness, profound adnyamia, sexual impotence, and advanced cachexia. X-rays showed a pituitary tumor the size of a small nut compressing the chiasma. The patient was subjected to radium treatment amounting in all to 7,360 mgm, distributed over eight seances in the course of four months. There was at first an aggravation of all the symptoms, but after about a month slow but progressive improvement set in, and finally a permanent clinical cure was established —Med Sci, 5, 309-310

(HYPOPHYSIS) Dystrophia adiposogenitalis Böge, München med Wehnschr, 1921, 68, 1668

This article describes a man of 24 with feminine habitus, macrosomia, adiposity, hypogenitalism, and defective development of the bones. The cause is perhaps a change of the pars anterior of the hypophysis. On the X-ray plate there is a shadow (tuberculoma?) in the place of the pars anterior —J K

(HYPOPHYSIS) The anencephalic syndrome in its relation to apituitarism Browne (F J), Edinb M J, 1920, N S, 25, 296-307

From the examination of five anencephalic monsters, Browne has come to the conclusion that the characteristic physical signs of anencephaly, apart from the absence of the brain and cranial vault, are connected with absence of the pituitary gland. These characteristic physical signs are as follows: (1) maldevelopment of the basis cranii, (2) protruding eyeballs, (3) protruding tongue, (4) aquilinity of nose, (5) large amount of cutaneous fat, (6) hyperplasia of the thymus, (7) small or absent suprarenal gland, (8) hyperplasia of the genital organs, (9) stunted growth of the trunk and limbs. Browne maintains that the internal secretions of the mother play no part, or at least a very minor one, in the development of the foetus, as they seem to have no effect in compensating for the secretions that are wanting in anencephaly. It is evident, also, that the endocrine glands of the foetus play an extremely important part in its development in utero —Med Sci, 5, 307

Oxytocic influence of extracts of HYPOPHYSIS and a new remedy, "Phvsormon" (Ueber die Art der Wechonanregung durch Hypophysenextrakte und über das neue Mittel Phvsormon) Calmann (A), Zentralbl f Gyn (Leipzig), 1921, 45, 1841-1842

The author tried unsuccessfully to initiate labor by the use of extract of hypophysis as recommended by Steig. However, excellent results were obtained when repeated injections in extremely small doses were made. "Phvsormon" is a preparation made from

the pars posterior and intermedia of the hypophysis It seems to be very active and may be used as a styptic as well as in amenorrhea Also in urinary retention and in paralysis of the bowels it seems to have a good effect It produces a very marked rise of blood pressure—J K

A case of tumor of the HYPOPHYSIS (Een geval van hypophysisgezwell) Carp (E A D E), Nederl Tijdschr v Geneesk (Haarlem), 1921, 66 (I), 350

The case is reported of a man of 33 who complained of bad vision and headaches, without vomiting He felt drowsy There was beginning adiposity, loss of sexual desires, and loss of hair, but no polyuria or increased sugar-tolerance Blood examination showed slight relative and absolute lymphocytosis An enlarged sella turcica with changes in the dorsum sellae was apparent on the x-ray plate—J K

(HYPHOPHYSIS) A case of pluriglandular insufficiency with acromegaly (Un cas d'insuffisance pluriglandulaire avec acromégalie) Caussimon (J), J de méd de Bordeaux, 1920, 91, 462-465

Caussimon, of Bordeaux, reports a case of acromegaly in a woman aged 36, associated with signs of pluriglandular insufficiency, viz, symptoms attributable to the thymus, thyroid, and ovary There was no enlargement or deformity of the sella turcica on x-ray examination Out of 33 cases of acromegaly collected by Caussimon from the literature between 1886 and 1919, in 26 no mention is made of persistence of the thymus, in 4 the presence of characteristic retrosternal dullness is noted, in 2 a persistent thymus was found, and in one no trace of it was present post-mortem The thyroid in these cases was sometimes atrophied and sometimes enlarged Occasionally there was exophthalmos In the present case there was definite atrophy of the thyroid, and the development of the subcutaneous tissue, appearance and texture of the skin, and scantiness of hair resembled those in myxoedema Disturbance of the ovarian function was shown by amenorrhoea which had been present from the onset, as in 30 of the 33 collected cases The present case did not show any symptoms attributable to the suprarenals, and in only two of the 33 cases was involvement of these glands noted Thus Motais states that his patient's skin became bronzed as in Addison's disease, and Gilbert Ballet and Laignel-Lavastine's case the suprarenals were found post-mortem to be full of adenomas—Med Sci, 5, 309

(HYPOPHYSIS) Defects in membranous bones, exophthalmos and diabetes insipidus an unusual syndrome of dyspituitarism Christian (H A), Med Clin N Am (Phila), 1920, 3, 849-870

Christlan, of Boston, records the case of a girl, aged 5, who presented the symptom-complex of diabetes insipidus associated with very extensive defects in the skull-bones and bilateral exophthalmos. Pituitary extract controlled the polyuria when given subcutaneously, but no other method of introducing pituitary substance had any effect upon the polyuria, and no method of giving pituitary substance had any influence on the bone defects or the exophthalmos. Only two similar cases have been recorded, viz, by Schuller, of Vienna, who, in a subsequent paper in which he comments on Christlan's case, comes to the conclusion that the syndrome is due to disease of the hypophysis, like acromegaly, dystrophia, adiposogenitalis, and pituitary dwarfism —Med Sci, 5, 399

La pathologie du naso-pharynx et des sinns sphénoïdaux contribue à la pathologie du système HYPOPHYSAIRE Citelli, L'oto-rhinolaryngologie internationale (Lyon), 1919, Reprint, 5 p

Citelli summarizes the work of himself and his pupils on the significance of the pharyngeal hypophysis. He believes that it is a functioning organ that shares in the activity of the hypophysis, proper, with which it is not infrequently connected by a persistent pharyngo-hypophyseal duct. Evidence is cited that the "hypophyseal system" may be affected by nasopharyngeal or sphenoidal sinus disease giving rise to a syndrome marked by mental sluggishness. This is frequently ameliorated by hypophyseal medication.

—R G H

On the PITUITARY active principles and histamine Dale (H H) & Dudley (H W), J Pharmacol & Exper Ther (Balt), 1921, 18, 27-42

These investigators agree with Abel and Nagayama that boiling with 0.5 per cent HCl destroys the pressor and oxytocic actions of pituitary extract. However, they find that the oxytocic substance is not completely destroyed by six hours' boiling. Moreover, the oxytocic action obtained from the substance remaining is much greater than that from histamine of equal depressor action. They see no reason to suggest a relation between histamine and the specific action of the extract. The specific oxytocic principle is slowly destroyed by erepsin —F A H

Characteristic effects upon growth, oestrus, and ovulation induced by the intraperitoneal administration of fresh anterior HYPOPHYSEAL substance Evans (H) & Long (J), Anat Record (Phila), 1922, 23, 19

Daily intraperitoneal injection of fresh anterior lobe of beef hypophysis causes acceleration of growth in white rats. Oral administration fails to do this. Oestrus may never occur or may be

exhibited only at long intervals Ovaries were always enlarged, showing much lutein tissue about unruptured normal follicles and atretic follicles Ripe, normal Graafian follicles were invariably absent —W J A

The secretory activity of the anterior lobe of the PITUITARY body during pregnancy (*Sull'attività secretiva della preipofisi in gravidanza*) Gentili (A), *Sperimentale*, Arch di biol (Firenze), 1920, 74, 286-291

Investigations were carried out by means of over 100 pituitary bodies collected from cows at different periods of pregnancy, as well as on many specimens from nulliparous animals The results obtained are in great part a confirmation of well known facts, and may be summarized as follows The anterior lobe of the pituitary body increases progressively in size and weight from the beginning to the end of pregnancy While the average weight of the hypophysis of nulliparous cows is from 135-140 mgm, it already reaches 170 mgm at the beginning of a first pregnancy, increasing up to 350 mgm at the end of it In cows of the same body weight, but multiparous, the weight of the pituitary body may increase from 310 up to 460 mgm This means that in proportion to the body weight that of the hypophysis grows from 1 100,000 in nulliparous cows to 1 50,000 at the end of the pregnancy in multiparous animals Histologically the anterior lobe of the pituitary body of pregnant cows forms an excellent material for the study of the so-called gravidic cells, the chief function of which appears to be the secretion of a progressively increasing amount of lipid substances belonging, according to the author, to the phosphatides Another feature of the anterior lobe of the pituitary body during pregnancy is the production of great quantities of colloid material, with the secretion of which the chromophobe cells appear to be chiefly concerned —Med Sci 4, 371

(HYPOPHYSIS) The pathology of dystrophia adiposo-genitalis (*Die Pathologie der Dystrophia adiposogenitalis*) Gottlieb (K), *Ergebn d allgem Path u path Anat* [etc], (Wiesb), 1921, 19, 575-650

The author reviews both the clinical and the experimental work on dystrophia adiposo-genitalis To study its pathogenesis in man he assembles from the literature the 87 cases in which autopsy findings are given, showing (1) Some disturbance in or in the region of the hypophysis, (2) adiposity, (3) usually genital atrophy From the analysis of these he concludes that the disease is due to an alteration or diminution in the hypophyseal secretion reaching the subthalamie centers Tumors, cysts or other pathological changes involving the whole gland or one of its lobes, also

external pressure from a neighboring tumor or from hydrocephalus may be the cause. He looks upon adiposity as an effect secondary to the alteration in the carbohydrate metabolism. The usual cases of complete destruction of the hypophysis without dystrophy he is unable to explain. A bibliography of 159 complete references is given —(D M) W J M S

(HYPOPHYSIS) Pathological anatomy and pathogenesis of dystrophia adiposo-genitalis (*Zur pathologischen Anatomie und Pathogenese der Dystrophia adiposo-genitalis*) Gottlieb (K), *Ztschr f ang Anat* [etc], (Berl), 1920, 7, 60-86

The clinical and detailed autopsy findings in three cases of dystrophia adiposo-genitalis and a short summary of nine other cases are compared with cases recorded by others with the following conclusions. The clinical picture in dystrophia adiposo-genitalis is primarily due to involvement of the hypophysis. The disturbance of the hypophysis may be due to some extrinsic cause, such as tumors, hydrocephalus, etc , as well as to some primary pathological change in the hypophysis itself. The association of the disease with a particular lobe of the hypophysis is not justified, for it may arise from dysfunction of the anterior lobe as well as from interference with the discharge of the secretion from the posterior lobe and the stalk. Both hypo-secretion and abnormal (false) secretion as a rule result in dystrophia adiposo-genitalis, unless the false secretion arises from an acidophilic change in the anterior lobe, in which case acromegly results. If the hypophysis undergoes great damage in early childhood, dwarfism results. There are a few cases in which no disease results in spite of these pathological conditions. Such exceptions are explained upon the assumption that there is a hyposensitiveness in these individuals to the hypophyseal hormone or there is but little dependence of the central nervous system on pituitary influence. Fifty-five references to literature are given

—A T R

Action of the HYPOPHYSIS on growth (*Action de l'hypophyse sur la croissance*) Houssay (B A) & Hug (E), *Compt rend Soc de biol* (Paris), 1921, 85, 1215-1218

Observations have been made on twelve lots of young dogs (5-10 dogs to a lot) since 1908. Careful controls were kept, some were operated upon without the removal of the hypophysis and others left normal. "Young dogs deprived of the hypophysis present a dystrophy which is not due to operative traumatism, and which is characterized by arrest of growth, adiposity, change in character, modification of the genital organs, thyroid and thymus "

—T C B

Meningeal relations of HYPOPHYSIS CEREBRI Hughson (W),
Anat Record (Phila), 1922, 23, 21

Study of serial sections of this region shows that in addition to the dural covering of the floor of the sella turcica, the hypophysis is completely surrounded by an arachnoid membrane continuous with that of the brain. Similarly the pia is reflected upon the hypophysis investing it closely. Between these two membranes is a space, traversed by many trabeculae so that it becomes close-meshed. The continuity of this leptomeningeal space about the hypophysis with the cranial subarachnoid space has been demonstrated by two methods of injection.—Author's abst

Adiposo-genital syndrome with HYPOPHYSIS tumors (*Le syndrome adiposo-génital dans les tumeurs de l'hypophyse*) Lereboullet,
Progrès méd (Par), 1922, 37, 52-55

Lereboullet reviews the current evidence on the symptomatology, etiology and treatment of Frohlich's syndrome.—R G H

Tardy infantilism in the adult of HYPOPHYSEAL origin (*L'infantilisme tardif de l'adulte d'origine hypophysaire*) Lereboullet
(P) & Mouzon (J), Paris méd, 1920, 11, 277-282

According to Lereboullet and Mouzon, tardy infantilism in the adult of pituitary origin, which was first described by Gandy in 1906, is characterized by the loss of sexual characters of adult life, viz, loss of sexual function and morphological retrogression of the primary and secondary sexual attributes. The syndrome occurs during the height of genital activity between 20 and 40, and particularly between 30 and 35. The accessory symptoms which are usually present, according to Gandy, are (1) some characteristics of myxedema, such as swelling of the face, dry and ichthyotic skin, and partial or total loss of hair (2) headache, sweating, polydipsia and polyuria, which often mask the onset of the symptoms, (3) gynecomastia, (4) smallness of the thyroid on palpation, (5) a previous history of syphilis. The syndrome is generally produced by a pituitary lesion, which may be due to adjacent bony lesions.—Med Sci, 5, 307

(HYPOPHYSIS) Incipient acromegaly in infancy (*Über das Vorkommen von Akromegalie im Kindesalter*) Petényi (G) & Jankovich (L), Monatschr f Kinderh (Leipz & Wien), 1921, 21, 14-21

Petényi and Jankovich record a fatal case of incipient acromegaly in a boy, aged 10½, who presented the characteristic facial appearance and thickening of the phalanges, though all the other typical symptoms of acromegaly, including psychical changes, were absent. Death was due to tuberculous meningitis. The autopsy

showed enlargement of the hypophysis, hyperemia of the anterior lobe, much increase in the eosinophil cells, and colloid change in the middle lobe. All the other endocrine glands presented a normal appearance, both on naked eye and on microscopical examination — Med Sci, 5, 308

Traumatic lesion of the HYPOPHYSIS and multiple paralysis of the cranial nerves (*Lésions traumatiques de l'hypophyse et paralysies multiples des nerfs crâniens*) Reverchon (L.), Worms (G.) & Rouquier, Presse méd (Par), 1921, 29, 742-743

The authors report a fatal case of fracture of the base complicated not only by paralysis of several cranial nerves (V, VI, and VII), but also by diabetes insipidus (polydipsia and polyuria), intense anaemia and asthenia, low blood-pressure, puerilism, and apathy. The autopsy showed that the condition was due to severe lesions of the hypophysis, which was reduced to a small fibrous nodule in which no trace of normal tissue could be found on histological examination. The case suggests that the hypophysis is injured more frequently than is supposed in fractures of the base either directly or indirectly, by compression by hemorrhage. The writers recommend that in fractures of the base one should look for evidence of diabetes insipidus as well as for the well-known signs accompanying this accident. X-rays will be of value in showing lesions of the posterior wall of the sella turcica — Med Sci, 5, 398

HYPOPHYSEAL cachexia due to acquired syphilis with cure (*Über hypophysäre Kachexie auf Basis von Lues acquisita mit Ausgang in Heilung*) Reye, Med Klin (Berl & Wien), 1920, 16, 1313-1314

Reye remarks that in addition to the two well-known types of pituitary disease, viz., acromegaly and dystrophia adiposo-genitalis, there is a third type which has been described by Simmonds, of Hamburg, under the name of cachexia of pituitary origin. It is characterized by severe cachexia with atrophy of all the organs, loss of teeth, eyebrows, eyelashes, axillary and pubic hair, as well as by psychical disturbance. This form of cachexia is caused by necrosis of the anterior lobe of the hypophysis, resulting from embolic processes occurring in the puerperium, and less frequently by malignant tumors or tuberculosis. Reye reports a case in a woman, aged 50, in whom the condition was due to acquired syphilis and was cured by antisyphilitic treatment. This is the first case on record in which pituitary cachexia was due to syphilis. In the seven other published cases of syphilis of the hypophysis (in six, congenital syphilis and in one, acquired syphilis) the clinical picture was that of dystrophia adiposo-genitalis — Med Sci, 5, 307

(HYPOPHYSIS) On the relative amounts of depressor and broncho-constrictor substance obtainable from the anterior and posterior lobes of the fresh pituitary gland Roca (J), J Pharmacol & Exper Ther (Balt), 1921, 18, 1-25

A blood-pressure lowering and broncho-constrictor substance was obtained from the posterior and anterior lobes of the pituitary gland by treatment with mercuric chloride in HCl By this method the pressor substance was removed The posterior lobe furnished seven to eight times as much depressor substance as an equal weight of anterior lobe A similar but somewhat greater ratio of the bronchoconstrictor substance was found in the two lobes Chloroform dissolves from suitably prepared material a substance acting like histamine on the arterial pressure, uterus and bronchi Chloroform takes up about twenty times more of this substance from the posterior lobe than from the anterior lobe, weight for weight The chloroform-soluble substance was thought to be histamine—F A H

The effects of PITUITARY extracts on the body temperature of animals rendered poikilothermous by destruction of the optic thalamus Rogers (F T), Proc Soc Exper Biol & Med (N Y), 1921, 10, 125-127

A series of pigeons was reduced to the poikilothermous condition by cauterization of the thalamus After death absence of any gross visible changes in the hypophysis was confirmed The organ in each of these animals had a perfectly normal appearance, although there may have been circulatory alterations or cytological changes invisible to the naked eye The injection intra-peritoneally of from 0.2 to 1.0 cc of pituitary extract (posterior lobe—Lilly) caused a sharp rise in body temperature Injection of the extract into normal birds causes no temperature reaction greater than the range of the diurnal variations In the poikilothermous pigeon the body temperature of which was artificially maintained at a normal level by keeping in a warm incubator, injection of pituitary extract was followed by a rise in temperature such as to threaten heat prostration The rise in body temperature persisted for twelve to twenty-four hours and then fell to a level determined by the environmental temperature The authors were unable to maintain the body temperature at the normal level by pituitary extract alone without the aid of the continuously warm incubator Frequently repeated injections of the extract led to the death of the animal, preceded by weakness and general prostration A number of quite different factors seem to be involved in this thermic reaction Further details and discussion will be presented later—R G H

Ocular symptoms in syphilitic **HYPOPHYSEAL** disease de Schweinitz (G E), Arch Ophth, N Y, 1921, 50, 203-217

De Schweinitz describes the ocular symptoms of hypophyseal disease in syphilitic subjects. He recognizes three groups of the disease. The first includes non-syphilitic pituitary disease in syphilitic persons. In the second the pituitary lesion is itself syphilitic. In the third group the hypophyseal disease occurs in the subjects of doubtful syphilis. The following case illustrates the first group. A man, aged 49 years, had demonstrable syphilis, with fine chorioidal changes. He suffered also from pituitary disease, as shown by the skiagraphic appearances of the sella turcica and bitemporal color hemianopsia. He complained of bad sight, headache and diplopia. Exophthalmos was present, as well as paralysis of the right external rectus and convergent squint. Sellar decompression, followed by the exhibition of pituitary body extract and specific treatment, resulted in considerable improvement. A second case was that of a man of 45, with a history of a primary syphilitic sore, who complained of diplopia and failing vision. There was paresis of the right external rectus and convergent strabismus. The field showed temporal color hemianopsia and other changes. Energetic specific treatment met with a prompt and satisfactory response. Later the patient neglected his treatment and had a relapse. On resuming treatment the result was satisfactory. In this case the pituitary lesion was itself syphilitic. The cases are also described of three women, who suffered from hypophyseal disease and were the subjects of doubtful syphilis. They were all treated with thyroid extract and pituitary body extract and with inunction of mercurial ointment. The results were good. The combination of these three agents appears to be a valuable one—Med J, Australia, 1921, ii, 356.

The effect of intraperitoneal injection of fresh anterior lobe substances in HYPOPHYSECTOMIZED tadpoles. Smith (P E) & Smith (I P), Anat Record (Phila), 1922, 23, 38.

Intraperitoneal administration of anterior hypophyseal substance has been found more effective in restoring the normal conditions in the pigmentary and endocrine systems and in the growth rate than administration by mouth—W J A.

Transplantation of the pars nervosa of the PITUITARY. Swingle (W W), Anat Record (Phila), 1922, 23, 125.

Subcutaneous homoplastic and heteroplastic transplantation of the pars nervosa of adult *Rana clamata* and *R. catesbeiana* into larvae causes shrinkage and emaciation after twelve hours. Control grafts of the pars anterior and brain tissue show no such effect. It is held that the shrinkage is due to the stimulation of the mesonephros to increased elimination of water—W J A.

(HYPOPHYSIS) Traumatic diabetes insipidus, successfully treated with pituglandol (Diabetes insipidus nach Trauma, erfolgreich mit Pituglandol behandelt) Thorner (W), Deutsche med Wchnschr (Berl), 1922, 48, 280-282

A man fell out of his aeroplane from a height of 500 meters, causing commotio cerebri without fracture of the skull After some days, polyuria and polydipsia were observed The blood had a high specific gravity (1064) with many erythrocytes (6,600,000) and hyperlymphocytosis The sugar tolerance was high and after injection of adrenalin, no glucosuria was seen Repeated injections of adrenalin slightly diminished the daily quantity of urine, but did not produce a rise of blood pressure Injections of pituglandol diminished the quantity of urine, though the concentration stayed low The blood became normal—J K

The influence of feeding anterior lobe of HYPOPHYSIS on growth and size of Amblystoma tigrinum Uhlenhuth (E), Anat Record (Phila), 1922, 23, 43

The author states that anterior lobe substance, when fed to metamorphosed Amblystoma tigrinum, causes an increase in the rate of growth and size, the animals becoming larger than those fed on other substances—W J A

The influence of feeding the anterior lobe of the HYPOPHYSIS on the size of Amblystoma tigrinum Uhlenhuth (E), J Gen Physiol (Balt), 1922, 4, 321-330

Amblystoma tigrinum fed on hypophysis of cattle grew much more rapidly than those fed on earth-worm, even up to 132 weeks The feeding of beef-liver as compared with hypophysis produces equally rapid growth but growth ceases much earlier—M E C

Over INFANTILISME de Vries (E), Nederl Tijdschr v Geneesk (Haarlem), 1922, 66, (I), 349

The author discusses the case of a girl of 17 with dwarfism, adiposity and a very defective development of the sex characteristics Only the skeleton is of the female type The girl is idiotic No other details are given—J K

Action of INTERNAL SECRETIONS on the iris Mazzei (A), Arch di ottal, 1918, Klin Monatsbl f Augenh, 1919, 62, 838-, Zentralbl Blochem Biophys, 21, 396-

Mazzei describes experiments with freshly enucleated frog eyes, one of which was placed in Ringer solution and the other in Ringer solution containing the substance to be tested Adrenaline, ovarin, endohypophysin and endothyreoidin caused dilatation of the pupil (most rapidly with adrenaline and most slowly with endothyreoidin)

Spermin caused rather prompt contraction of the pupil. In the case of simultaneous action of various hormones those with mydriatic effect usually acted less rapidly than those with myotic effect, e g., 5 drops of a mydriatic extract plus 3 drops of spermin caused slight myosis during the first few seconds, and this was followed by mydriasis after a few minutes. The slight myotic effect of spermin was inhibited by adrenaline, ovarin, thyreoidin and hypophysin and seldom had a predominant influence under such conditions—Chem Abst 14, 34

Pernicious anemia and INTERNAL SECRETION (Perniziose Anämia, Konstitution und innere Sekretion) Schauman (O), Ztschr f ang Anat [etc] (Berl), 1920, 6, 258-288

The author maintains that the idea that pernicious anemia has as a basis certain constitutional anomalies, is becoming more generally accepted. The literature and a few cases of his own are analyzed from this point of view. He concludes that at the bottom of pernicious anemia are anomalies of the endocrine system as well as of the bone marrow. For example, he thinks it not unreasonable to consider that the pigmentation is due to functional or structural changes in the suprarenals or chromaffin system. Individual differences in the clinical picture are considered to be due not only to differences in the external exciting cause, but also the variability in the inherent ductless gland pattern of the individual. Some of the factors, those which are responsible for the blood changes, are always present, others, such as those responsible for achylia, are less regularly present, while still others (those responsible for renal disease, spinal cord symptoms, abnormal pigmentation, psychic disturbances, cardiac hypertrophy, abnormal pigmentation, etc) are only occasionally in evidence. An extensive list of references is given.

—A T R

(MAMMA) Mastitis adolescentium [Zur Frage der akuten schmerzhaften Brustdrüsenschwellung grosserer Kinder ("Mastitis adolescentium")] Stern (G), Ztschr f ang Anat [etc] (Berl), 1920, 6, 367-374

Because of the neurasthenic manifestations, it is argued that a constitutional neuropathy is a primary factor in mastitis of adolescent children. The endocrine metabolic disturbances are considered secondary to these nervous components. A few references to literature are given—A T R

Opothérapie and the MENOPAUSE (Opothérapie et ménopause)
Opothérapie and minor Graves' disease (Opothérapie et petit Basedowisme) Marie (A) & Fourcade, Bull Soc de thér (Par), 1921, 4, s 26, 52-56, 176-178

Marie and Fourcade state that suppression of the monthly periods is not the only cause of such mental disorders at the menopause as obsessions, phobias, melancholia, acute hallucinations, and more or less systematized persecutorial insanity which occurred at this time. They were inclined to assign the chief rôle to endocrine insufficiency, especially of the thyro-ovarian secretion. They therefore made a systematic use of opotherapy in all the mental disorders of the menopause. After a preliminary period of 10-15 days devoted to a general disintoxication, when a slight degree of hepato-renal intoxication was present, a combination of thyroid and ovarian extract was employed, supplemented by suprarenal extract or extract of other endocrine organs whenever signs were present indicating their insufficiency. The histories of eight cases are recorded, in six of which considerable improvement took place under this treatment and in two no result was obtained. Subsequently Marie and Fourcade reported 10 cases with minor signs of Graves' disease that were benefited by pluri-glandular opotherapy consisting in administration of extracts from the ovaries, corpus luteum and hypophysis —Med Sci, 5, 309

(ORGANOTHERAPY) A suggested form of treatment for mental deficiency in children. Miller (J. A.), New York M J, 1921, 114, 231-232

The author assumes that the rather prevalent and wide attempts to treat mental deficiency in children with glandular extracts is irrational. "We cannot stimulate a dead body or an absent one"—H W

(ORGANOTHERAPY) The treatment of the vomiting of pregnancy by thyro-ovarian opotherapy (*Le traitement des vomissements gravidiques par l'opothérapie thyro-ovarienne*) Naamé, Bull Soc de thér (Par), 1921, 4 s 26, 180-182

According to Naamé, of Tunis, the vomiting of pregnancy is due to autotoxemia caused by thyro-ovarian insufficiency, and the cessation of vomiting towards the middle of pregnancy is the result of establishment of glandular equilibrium owing to hypertrophy of the thyroid. A rapid cessation of vomiting can be effected by thyro-ovarian opotherapy, which favors the development of this hypertrophy. The treatment consists in administration of tablets containing thyroïdine 0.05 gm and ovarian extract 0.10 gm, three times a day for a few days —Med Sci, 5, 310

OVARY grafting in clinical practice (*Over de klinisch overplanting van ovarium weefsel*) de Bruyne (F.), Vlaamsch geneesk Tijdschr (Gent), 1922, 3, 37-39

To diminish as much as possible the complaints after hysterectomy and after complete ovariectomy the author recommends the

transplantation of a piece of ovary subcutaneously This does not give as splendid results as the transplantation in the peritoneum, but when for one reason or another the graft must be removed no laparotomy is necessary In ± 50 per cent of the cases the graft disappears, in the other cases the issue grows and forms cysts When only corpus luteum is transplanted, hypertrophy is rare, transplantation of the cortex gives most cases of hypertrophy Transplantation of corpus luteum alone very seldom has any influence on the climateric complaints, when the graft consists of the cortex only, it nearly always has a very good influence on these symptoms Therefore it is of special importance that the graft contain a large quantity of cortex tissue —J K

Transplantation of OVARY (Overientransplantation) Fleischmann (K), *Deutsche med Wchnschr (Berl)*, 1922, 48, 245

A short article The indications for operation were amenorrhea, sterility and vasomotor disturbances The author does not state whether the operation was successful —J K

The comparative value of whole OVARIAN extract, CORPUS LUTEUM extract, and ovarian residue in menstrual disorders Hirst (J C), *N York M J*, 1921, 114, 391-394

The extract of the whole ovary is most useful in the treatment of the menopause, both natural and surgical, and the late establishment of menstruation The best method of administration is by deep muscular or intravenous injection Nausea is a common complaint following administration by mouth If the extract is given by mouth the dose should be five grains three times a day midway between meals, combined with one-fortieth of a grain of strychnine sulphate When ampoules are used the amount should be 10 cc to each injection (intramuscular) daily for thirty-six doses The series may be repeated after one or two months, if necessary The intravenous injection is preferable at times because of the rapidity with which adequate amounts can be given and the absence of local reactions Certain protein-sensitive individuals will show some systemic reactions, such as diffuse patches of erythema, urticaria and occasionally headache The indications for the use of ovarian residue are late development of puberty, infantilism, irregular menstruation at puberty, menorrhagia of puberty, obesity and amenorrhea-dystrophia adiposo-genitalis The methods of administration of ovarian residue are the same as those for whole ovarian extract "The results of this extract are still in the nebulous stage, as far as proof is concerned" Corpus luteum is used to control the nausea of pregnancy, habitual abortion without demonstrable cause, menopause (in which it is not as efficient as ovarian extract), scanty menses or functional amenorrhea of youth, pruritus vulvae or krau-

rosis vulvae in elderly women, and sterility The administration of corpus luteum is the same as for the two preparations mentioned above The nausea of pregnancy is relieved by a series of 12 intramuscular or intravenous doses in mild cases or two doses daily of 20 cc amounts in severe cases The presence of goiter in early pregnancy absolutely contraindicates the administration of corpus luteum extract, either intravenously or intramuscularly " Every such patient has been made worse by this treatment "

—H W

(OVARY) The existence of yellow atretic bodies in the interstitial gland of the rabbit (*Sur l'existence de faux corps jaunes autonomes dans la glande interstitielle de la lapine*) Salazar (A), Anat Record (Phila), 1922, 23, 189-193

The author calls attention to the existence in the ovary of the rabbit (ovary of the interstitial type) of yellow atretic bodies, with autonomous evolution, these, unlike the ordinary atretic bodies, do not amalgamate in the interstitial gland, but pass through their evolution autonomously, isolated within a connective-tissue capsule The author briefly describes their characteristics and admits the possibility of their being confused with genuine old yellow bodies, this confusion being possibly one of the causes of the contradictory opinions that have been formulated with regard to the regression of the real bodies —Abst, Wistar Institute

Function of the OVARY during gestation (*Fonctionnement des ovaires pendant la gestation*) Vignes (H), Progrès méd (Par), 1922, 37, 49-52

A review of the literature leads the author to the following conclusions The ovaries increase in size during gestation, the corpus luteum becomes harder and larger than it is at the time of menstruation, and there are a considerable number of follicular atresias Ovulation is usually suspended, but there are exceptions to this rule, the function of menstruation ceases during gestation The secretion from the ovary acts upon the mucous membrane of the uterus to bring about premenstrual congestion, the condition necessary to nidation For a certain length of time the ovary keeps the mucous membrane of the uterus in a condition which is indispensable to the development of the embryo This sensitization of mucous membrane and this role of protection are attributed particularly to the corpus luteum Injury to or disfunction of the ovary may cause pathological conditions in the course of gestation —R G H

(OVARY) Dysmenorrhea Young (J Van D), N York M J, 1921, 114, 395-397

True dysmenorrhea may be looked upon as the result of two conditions (1) a deficient ovarian function associated with a normal

myometrium—a condition which permits of a profuse clotted flow, (2) a degenerated uterine wall which causes a mechanical barrier to uterine circulation—a condition which produces a scanty flow and cramps Pain in the first condition may be looked upon as the result of unhormonized blood clotting (normal menstrual blood does not clot and will prevent other blood from clotting), and in the second condition to muscular spasms In either condition the endometrium has no part in the causation of pain, the endometrium seldom is a causative factor in dysmenorrhea The author has devised a treatment which consists in the production of rhythmical uterine stimulation on the Bier's hyperemia principle—H W

The internal secretion of the PANCREAS Banting (F G) & Best (C H), J Lab & Clin M (St Louis), 1922, 7, 251-266

The authors attempted to secure extracts of Langerhans islet tissue from the pancreas in the hope that it would give hormone effects uncomplicated by the action of enzymes It was found that intravenous injections of extract from dog's pancreas, removed from seven to ten weeks after ligation of the ducts, invariably exercised a reducing influence upon the percentage of the blood sugar and the amount of sugar excreted in the urine Rectal injections were not effective The extent and duration of the reduction varied directly with the amount of extract injected Pancreatic juice destroyed the active principle of the extract That the reducing action was not a dilution phenomenon was indicated by the following facts (1) hemoglobin estimations before and after administration of extract were identical, (2) injections of large quantities of saline solution did not effect the blood sugar, (3) similar quantities of extracts of other tissues did not cause a reduction of blood sugar Extract made 0.1 per cent acid was effectual in lowering the blood sugar The presence of extract enabled a diabetic animal to retain a much greater percentage of injected sugar than it otherwise would Extract prepared in neutral saline solution and kept in cold storage retained its potency for at least seven days Boiled extract had no effect of reduction of blood sugar—R G H

The thermostable active agent of pig's PANCREAS Jones (W), J Biol Chem (Balt), 1922, 50, 322-328

Not of endocrine interest—F S H

The internal secretion of the PANCREAS (*La sécrétion interne du pancréas*) Waterman (N), Arch néerl de physiol, 1920, 4, 289-346

Alcoholic extracts of the pancreas and the change in viscosity of blood are used as a measure of the lipins The internal secretion of the pancreas consists in the production of a complex lipid, an

unstable lipoid-phosphatide, which dissociates and liberates free fatty acids This lipoid influences the permeability of the cellular membranes, it regulates glycogenesis and the excretion of sugar by the kidney The factors which influence the dissociation of this complex lipoid, and likewise the formation of intermediary compounds of carbohydrates, are heat, adrenaline and chloroform—Chem Absts 14, 2945

Transplantation of PARATHYROIDs in post-operative tetany
(*Epithelkorperverspflanzung bei postoperativer Tetanie*) Borchers
(E), Munchen med Wchnschr, 1921, 68, 1609-1612

It is not always possible to avoid post-operative tetany because (1) in goiter the parathyroids are often not normally situated, (2) the parathyroids mainly get their blood from the inferior thyroid artery, which must be ligated for the operation, (3) when malignant growths are present it is impossible to avoid removing the parathyroids Often the first symptoms of tetany are observed only many weeks after the operation Homoioplastic transplantation of parathyroid and histological examination before transplantation are necessary to make sure that the organ is a real parathyroid Such transplantation may give splendid results though it is not always successful The author quotes a case of a woman who was operated upon in 1882 and who died in 1919 At post-mortem examination it was found that a parathyroid that had been grafted into the liver was perfectly normal and had even become larger

—J K

(PARATHYROID) An undescribed condition of infancy and its treatment Clark (G H), Glasgow M J, 1920, 94, 193-202

Clark, of Glasgow, describes two cases in children aged 15 months and 2½ years whose principal symptoms were idiocy, depression, fibrillary twitchings in the muscles, jerking movements in the limbs, convulsions and inability to balance Considerable improvement took place in both cases under treatment with parathyroid gland tablets The symptoms were very similar to those observed by Paton and Findlay after thyro-parathyroidectomy in animals, hence Clark's cases were probably examples of parathyroid tetany—Med Sci, 5, 305

(PARATHYROID) Du rôle du calcium dans la tétanie Kummer
(H), Presse méd (Par), 1920, 28, 765-766

The cases are reported of two patients in whom the ingestion of citric acid brought on severe attacks of tetany This effect is ascribed by the author to calcium deprivation due to the formation of calcium citrate He believes that calcium depletion deprives the body cells of defense, leaving them more vulnerable to the toxin that brings about parathyroid tetany—R G H

The prevention and control of PARATHYROID tetany Luckhardt (A. B) & Rosenbloom (J), Proc Soc Exper Biol & Med (N Y), 1921, 19, 129-130

To test the hypothesis that parathyroid tetany is due to accumulated toxin, the authors determined the effect of copious diuresis on the process Ringer's solution or the same without calcium was injected intravenously in amounts of 33 cc or more per kilo. Animals were kept alive in good state of nutrition for long periods (up to 51 days). Typical tetany supervened when diuresis was discontinued and meat diet maintained. The presence of calcium in the injected fluid appears to have been of little significance —R G H

Transplantation of PARATHYROID in paralysis agitans (Behandlung des Paralysis agitans mit Epithelkörperimplantation) Su-deck, Deutsch med Wehnschr (Berl), 1922, 48, 210

The effect of this operation is due only to suggestion —J K

(PARATHYROIDS) Calcium metabolism in tetany Underhill (F P), Tileston (W) & Bogert (L J), J Biol Chem (Balt), 1922, 50, xxxix.

When compared with normal individuals under the same experimental conditions a subject with tetany, presumably of gastrointestinal origin, showed a normal type of behavior to calcium intake except that there was evidence of a greater tendency to store calcium temporarily on a calcium-rich diet. On the other hand, on a calcium-poor diet this stored calcium was eliminated to a much greater extent than occurred in the normal subject. These facts may, perhaps, be interpreted to mean that the organism with tetany shows a greater need for calcium than the normal individual, but that in tetany the regulation of calcium equilibrium is in an unstable condition —F S H

Mixed tumor of the PINEAL gland (Ein Beitrag zu den Mischtumoren der Zirbeldrüse) Frank (M), Ztschr f ang Anat [etc], (Berl), 1921, 8, 65-78

Detailed description of autopsy findings in a 20-year-old man with a large (34x24x22 mm) mixed and partly cystic tumor of the pineal gland. Literature —A T R

Un cas de SCHLERODERMIE Hugel, Réunion dermatologique de Strasbourg, Jan 8, 1922, abst Presse méd, 30, 154

The case was presented of a man of 45 who showed marked scleroderma of the lower limbs. The condition was ameliorated by the use of "fibrollysine" supplemented with pluriglandular organotherapy —R G H

SCHLERODERMIE et opothérapie associée Lereboullet (P), Bull et mém Soc méd d hôp de Par, 1921, 3 s, 45, 1200-1204

Lereboullet reports three cases showing the benefit obtained in cases of scleroderma by the association of thyroid, pituitary, and suprarenal extracts—Med Sci, 5, 310

Antitoxic action of SECRETIN from spinach for strophanthin (Ueber die entgiftende Wirkung der Spinatsekretinlösung auf Strophanthin) Miyadera (K), Deutsche med Wchnschr (Berl), 1922, 48, 313

When secretin, extracted from spinach as described by Bickel, was added to strophanthin the toxicity of this substance was largely decreased—J K

A suggestion as to the cause of the aspermatic condition of the imperfectly descended TESTIS Crew (F), J Anat & Physiol (London), 1922, 56, 98-106

The author holds that the imperfectly descended testis is aspermatic because the temperature of the abnormal position is higher than that which is normal for the scrotum. The latter is conceived to be the optimum temperature at which the final stages of spermatogenesis take place—W. J A

Hypoplasia of the TESTES during the period of development (Über die hypoplasie der Hoden in der Entwicklungsperiode) Diamantopoulos (S), Ztschr f ang Anat [etc], (Berl), 1921, 8, 117-154

Ninety-nine pairs of testes from new-born (some premature and some full term) to boys 18 years of age, were examined histologically. The normal testis at birth has wide tubules and practically no interstitial tissue. Testes with narrow tubules and interstitial tissue are considered underdeveloped. Of these 99 pairs, 60 were underdeveloped (37 very pronounced and 23 only slightly). Two of these undeveloped testes had no interstitial cells while in the rest this tissue was moderate or small in amount. No direct relationship was found between development of the tubules and amount of interstitial tissue. Puberty apparently brings many of these undeveloped testes nearly up to normal. Of the 34 cases of status lymphaticus and thymolymphaticus, 21 had underdeveloped testes and in 13 they were normal. Seven cases showed, besides abnormal sexual development and status lymphaticus, suprarenal hypoplasia (4 with both cortex and medulla and 3 with only cortex). There were 5 cases with hyperdevelopment of the thyroid. Boys with underdeveloped testicles are less resistant to infections and other disturbances, which probably explains the large number of cases of hypogenitalism in dead children. Hypoplasia of the testes

inhibits the growth of the prostate and seminal vesicles Diseases of the mother had apparently no bad effect on the testes of the fetus A long list of references is given —A T R

Proliferation of the interstitial cells in chorioneplithelioma of the TESTIS (Über Wucherung der Leydig'schen Zwischenzellen bei Chorioneplitheliom des Hodens) Hedinger (E), Ztschr, f ang Anat [etc], (Berl), 1920, 7, 55-59

The case is that of a 29 year old man who died from multiple metastasis one month after the right testis had been removed because of a chorioneplithelioma of the right testis The left testis was found to be normal except for a great increase in the interstitial cells as compared with the testes of about 100 influenza cases between 25 and 35 years old, which the author used as control material In three cases (soldiers from 25 to 35 years of age) of unilateral castration of long standing there was no such increase in the interstitial cells of the remaining testis Attention is drawn to a similar situation in the female where chorioneplithelioma of the uterus is related to proliferation of lutein cells in the ovary No literature —A T R

(TESTES) Partial castration (Sur les conséquences de la castration partielle) Lipschütz (A), & Ottow (B), Compt rend Soc de biol (Par), 1920, 83, 1340-1341

As a result of studies on a rabbit and three guinea-pigs the authors conclude that a small remaining fragment of a normal testis ($\pm \frac{1}{10}$ the normal weight) can furnish the organism the quantity of internal secretion necessary to the development of normal sexual characters But a diminution of the quantity of the internal secretion during the development of the organism can result in retardation of development of the sexual characters If only a part of the testis is left augmentation of the total weight of the rest of the testis does not take place It is very probable that the germinative tissue in the testis is in a state of degeneration as after the ligation of the vas deferens It is very probable that the interstitial tissue in the divided testis is increased in size That is why the number of interstitial cells, the cells in which internal secretion is formed, is not very much decreased in partial castration —R G H

So-called mixed-tumors of the TESTICLE (Sui cosiddetti "tumori-misti" del testicolo) Renato (M), Morgani (Milano), 1921, 64, 375-385

Of no immediate endocrine interest —J K

Transplantation of TESTICLE (Hodcnuberpflanzung) Rosenthal (H), Deutsche med Wchnschr (Berl), 1922, 48, 209

A short article An operation is indicated in very few instances, desire for rejuvenation is no indication In Germany there seems to be a regular trade in testicles, some persons offering to sell one of theirs —J K

The supposed relation between alkalosis and TETANY and similar conditions Greenwald (I), Proc Soc Exper Biol & Med (N Y), 1921, 18, 228-234

This is a technical discussion of literature and of personal findings Doubt is cast upon the current hypothesis that alkalosis may form an important part in the genesis of tetany

—R G H

(THYMUS) Observations on the effect of hyperthymisation (*Beobachtungen über die Folgen der Hyperthymisation*) Demel (R), Mitt a d Grenzgeb d Med u Chir (Jena), 1922, 34, 437-449

The author removed the thymus from rats of 3 weeks, 2 months and 8 months, respectively, and transplanted the organs into young rats After the grafting marked adiposity developed and the animals were very lively and vigorous The growth of the bones in length increased after implantation of a thymus The thymus of animals of 3 weeks or 2 months is more active than the thymus from rats of 8 months Even the influence of the thymus from other animals cannot be denied The epiphyses of the bones of the rats in which the thymus is implanted is broader than in control animals The structure of the bone becomes much more compact after implanting a thymus The transplantation has no influence on *adrenals*, *gonads* or *hypophysis* Administration of thymus by mouth has no influence on rats —J K

Congenital bone fragility and the THYMUS Contribution to the study of bone dystrophies in relation to the endocrine glands (*Fragilità ossea congenita e timo Contributo allo studio delle distrofie ossea in rapporto con le ghiandole endocrine*) Frontali (G), Riv di clin pediat (Firenze), 1920, 18, 257-309

After a critical review of the literature of the subject, the author describes a case of congenital bone fragility, which has been studied in detail with all applicable modern methods The child was observed between her first and third months of life A first fracture was noted immediately after birth The skull was of parchment consistency The lower limbs were shorter than normal (18 26 5 cm) and there were numerous callosities on all tubular bones Blood examination showed red corpuscles, 3,624,000, haemoglobin, 80%, white corpuscles, 7,500, lymphocytes, 63 5%, transitional forms, 3 5%, neutrophile polynuclear cells, 25%, eosinophiles, 1%, basophiles, 0 5% Galvanic excitability of several

muscles was found diminished, with little difference between anode and cathode, sometimes the formula was inverted. Calcium retention for 3 days averaged 26%, the calcium content of the blood (weighed as CaO) was 0.2866%, both being approximately normal. Radioscopy showed bone translucency increased throughout, the delicate outline of the cortex was partially interrupted, epiphyseal lines were normal.

Death from pneumonia occurred and a necropsy was made. The thymus was reduced in volume and weight (3gm), grey in color, and sclerotic. The total number of bone fractures was 33. In tubular bones the epiphyseal ossification zone was normal, the compact layer, completely missing. It appeared as though absorption of the embryonic fibrous bone tissue had failed to occur. There was no cortical compact layer, but a calcification of the thickened periosteum. Numerous other details as to bone are recorded. In the thymus connective tissue was considerably increased. Groups of epithelioid cells and of Hassall corpuscle were isolated by fibrillar rings. The internal structure of the lobuli showed a diminished number of epithelioid cells with poorly stained protoplasm—in short, sclerosis with lymphoid degeneration and atrophy of the epithelioid elements. The thyroid was slightly hyperplastic but otherwise normal as were the hypophysis and adrenals. The degeneration of the thymus is considered as etiologically related with the bone dystrophy. Congenital fragility of the bones, a definite entity of prenatal origin, must be differentiated from such conditions as rickets, etc. The cases in the literature which were not complicated by rickets were characterized by severe periosteal aplasia. The case described showed a complete absence of compact cortical bone and other evidence of insufficient activity of osteoblasts. Osteoclasts were rare. Therapeutic injections of serum of children with normally functioning thymus is proposed.—Author's abstr. abbreviated.

Variations in the form and position of the THYMUS (Über Variationen der Thymusform und -lage). Gruber (G. B.), *Ztschr f ang Anat* [etc.] (Berl.), 1920, 6, 320-332.

Description and 13 illustrations of various types of persistent thymus found in new-born and very young children, with a discussion of their rôle as mechanical factors in so-called thymic death. It is considered possible that this might be brought about by compression of the large vessels and trachea. Further investigation is considered necessary to decide whether hyperplasia of the thymus is always the pathologic-anatomical equivalent of hyperthymization. Some references to literature are given.—A. T. R.

Lymphosarcoma of the THYMUS [Lymphosarcome du thymus (Présentation de pièces)]. Harvier (P.), *Bull et mém Soc méd d hôp de Par*, 1921, 3 s 45, 374-378.

Harvier reports a case of lymphosarcoma of the thymus in a woman aged 25, characterized by a syndrome indicating compression of the superior vena cava, and consisting in cyanosis of the face, edema of the front of the thorax, extraordinary development of the collateral venous circulation from the face to the pubes, as well as in a continuous cough, with attacks of suffocation and intermittent pain in the left shoulder and arm. Physical examination showed retrosternal and left subclavian dullness, left pleural effusion, no cardiac symptoms except permanent tachycardia, and no signs of bronchial compression. Death took place eight months after the first symptom, and the autopsy confirmed the diagnosis of a large tumor of a sarcomatous nature occupying the region of the thymus and involving secondarily the lungs, heart, diaphragm, liver, and kidneys —Med Sci, 5, 305-306

The influence of THYROID gland feeding upon tadpoles from which the thyroid gland and the buccal anlage of the HYPOPHYSIS have been removed Allen (B M), Anat Record (Phila), 1922, 23, 101-102

Experiments were performed upon *Rana sphenoccephala* (1) Normal controls, (2) controls cut as for hypophysis removal, (3) thyroidless tadpoles, (4) those deprived of the buccal anlage of the hypophysis, (5) tadpoles deprived of both thyroid and buccal anlage. All were fed weighed quantities of sheep thyroid preparations. The purpose was to determine whether the influence of thyroid feeding would be the same in each case. Tadpoles in young feeding stages were employed in lots of twenty-five. It appeared that presence or absence of these glands in the tadpoles had little control upon the influence exerted by thyroid feeding upon limb development. The tail was not so quickly reduced as a result of administration of thyroid to groups 4 and 5 as in groups 1, 2 and 3. It is possible that future experiments in administering more diluted doses of thyroid preparations may prove a more delicate test. A study of the thyroid glands of controls and of tadpoles deprived of the buccal anlage of the hypophysis fails to show any modification of gland development or of colloid accumulation to result from thyroid feeding—Author's abstr

(THYROID) The use of radiotherapy in Basedow's disease (La radiothérapie dans la maladie de Basedow) Bécélère, J méd franç (Par), 1920, 9, 302-305, Arch d'électric méd (Par), 1920, 28, 348

Radiotherapy is the ideal treatment for Basedow's disease and for all forms of hyperthyroidism, for, better than intervention, it destroys the secreting elements, or, at any rate, diminishes their secretory activity. When the morbid condition does not date back more than a year and the gland is soft, treatment by intensive doses

at long intervals takes only from two to three months. In chronic forms, with a hard gland to which are added hyperplastic lesions of the connective tissue, the treatment takes at least six months, and improvement remains incomplete. In simple hyperthyroidism, on the contrary, radiotherapy is always perfectly successful, but it is in serious forms with extreme wasting and intense rapidity of heart action that this method gives the best results. Irradiation should be penetrating (20 cm equivalent spark gap, 5 mm aluminum, 20 cm distance from the anticathode, localizing cylinder 10 cm in diameter), sances should be weekly, and the dose 3H. Radiotherapy should be directed towards the function and not towards the lesion, and should be guided by the disorders of circulation (frequency and inequality of the heart-beats) and avoid substituting for excess, a deficiency of the thyroid secretion — Med Sci, 4, 390-391

(THYROID) On a further series of 500 goitre operations with special reference to after-results. Berry (J), Proc Roy Soc Med (Lond), 1921, 14, (Surg Sect) 89, Brit J Surg (Bristol), 1920-1921, 8, 413, Abst, Med Sci (Lond), 1922, 5, 324-325

Berry devoted this paper to a careful review and analysis of his cases, including all in which he had removed any portion of the thyroid gland during the period from 1913 to 1919, inclusive. The cases were 500 in number and formed a direct continuation of a previous series. Only about 12.5 per cent of the patients were males, and the age at which the disease was most common was between 30 and 50. Five girls, however, were only 14 years old. These were all examples of parenchymatous goitres which were causing dyspnoea and failing to respond to medical treatment. Operations in children below the age of puberty were hardly ever necessary and should never be undertaken except for some specific reason. Among the male patients, 7 were over 70 years of age, and all made good recoveries. One hundred ninety-eight cases were encapsulated lesions, adenoma, or cysts, and 302 were non-encapsulated. These included 13 examples of malignant disease. Berry states that pathologically the above classification is not strictly accurate, but is convenient, clinically. He lays stress upon the inefficiency of modern classifications, but points out that the terms in use are of clinical value. The series includes only 3 cases of inflammation. There were, however, 79 operations for exophthalmic goitre, and he points out that these cases should be sharply distinguished from false exophthalmic goitres, that is, localized lesions which may give rise to tachycardia and tremor but never show any exophthalmos. Of the malignant cases some were of the papilliferous variety, one was an endothelioma, and two were sarcomata. In this group the first sign for operative interference was dyspnoea, 74 operations being undertaken for this cause. Dis-

comfort and deformity or hyperthyroidism were the next most frequent indications. He points out that dyspnoea, when long persistent, may lead to other complications, such as dilation of the heart, tachycardia, and chronic lung trouble. In no case had he to perform a tracheotomy, as he holds very strongly that the removal of the source of the pressure, namely, the goitre, is a far more satisfactory procedure. He points out, however, that after the goitre has been removed there is sometimes a danger of tracheal collapse. When the trachea is bilaterally compressed the removal of one lobe may be quite insufficient to relieve the dyspnoea or indeed may make it worse, as this may lead to kinking, which usually causes fatal suffocation. He also points out that a unilateral enlargement of the thyroid may be considered the cause of the dyspnoea, whereas the opposite lobe, which may be the real offender, may lie deep behind the sternum within the thorax. He lays stress upon the difficulties of diagnosis in doubtful malignancies and states that a positive diagnosis of malignancy is almost impossible, although there may be points which give rise to suspicion. It is important, in making a diagnosis, to determine whether the thyroid moves upon the larynx or the trachea, for in the malignant cases it is likely to be fixed. He gives a full review of the operations which have been undertaken for the different varieties of disease and also a full description of his method of removing an intrathoracic goitre. In nearly all cases drainage was employed, being omitted in only 7 of the 500 cases. There were only 2 deaths in the simple goitres, 3 in the exophthalmic goitres, and 2 in the malignant diseases. Of the 500 cases he had traced all but 14 cases. Of the total, 342 of the simple goitres, 53 of the exophthalmic goitres and 5 of the malignant cases were quite well.—R. G. H.

The fundamental classification of THYROID disease by the basal metabolic rate. Boothby (W. M.), Collected Papers Mayo Clinic (Phila.), 1921, 297-303, reprinted from J. Am. M. Ass. (Chicago), 1921, 76, 84-86.

The measurement of the heat production in an individual under standard conditions serves to differentiate diseases into three groups: those with decreased, those with increased, and those with normal basal metabolic rates. The value, the limitations, and the essentials of technic and physiologic details are discussed.—J. F.

(THYROID) Total metabolism in exophthalmic goitre. Boothby (W. M.) & Sandiford (I.), J. Biol. Chem. (Balt.), 1922, 50, xlvii.

The work included a quantitative study of the food intake, urinary elimination, the blood chemistry, and the respiratory metabolism in three cases of exophthalmic goitre. The total metabolism was found to be frequently in excess of 5,000 calories per day and occasionally over 6,000 calories, which is in marked contrast to the

daily food ration of 1,500 to 1,800 calories common in many countries during the war—F S H

(THYROID) Sloughing cornea in Graves' disease and in disseminated sclerosis Buller (T H), Brit J Ophth, 1921, —, — (July)

Buller describes the case of a woman suffering from exophthalmic goitre, who had such exaggerated proptosis that the left cornea could not be covered by any effort. She rejected his advice to have the lids sutured together and a month later was seen with an infiltrated anesthetic cornea, which soon developed an ulcer and onyx. The cornea was incised and the lids sutured. In two days the sutures cut out and the eye re-opened. Cauterization failed to check the spread of ulceration and the eye was finally enucleated. The second cornea began to ulcerate, but the patient by this time was very low and soon died of heart failure—Med J Australia, 1921, II, 356

THYROID opotherapy and tuberculosis (Opothérapie thyroïdienne et tuberculose) Coulaud (E), Ann de méd (Paris), 1921, 10, 385-394

Evidence is presented from a series of 7 cases that thyroid therapy is distinctly harmful in pulmonary tuberculosis—F S H

The reticular material as an indicator of physiologic reversal in secretory polarity in the **THYROID** cells of the guinea-pig Cowdry (E), Am J Anat (Phila), 1922, 30, 25-37, Anat Record (Phila), 1922, 23, 13

In the thyroid glands of normal guinea-pigs, the reticular material (i e., Golgi apparatus, canalicular apparatus, etc.) is not invariably found between the nuclei and the follicular lumen, as is generally supposed. In some cases it undergoes an active migration to the opposite pole of the cell, which, together with other evidence at hand, indicates the existence of a reversal in physiologic polarity whereby the secretion is discharged directly into the circulation, instead of being first stored within the follicles—Author's abst

(THYROID) Cretinism—early diagnosis Echols (G L), J M Ass Georgia (Atlanta), 1921, 10, 825-826

Echols emphasizes the desirability—and infrequency—of early diagnosis of cretinism to permit most successful treatment and forestall feeble-mindedness and insanity in later years. The symptoms regarded as most important are (1) protrusion of tongue, (2) yellowish skin, loose and wrinkled (especially forehead), often some puffiness of the features with thickening of the eyelids, nos-

trils and lips, also of hands, feet and back of neck, due to myxoedematous swelling, (3) abdominal swelling, (4) general mental apathy and slowness of movement, (5) scantiness of hair and eyebrows, (6) snorting and snoring breathing, (7) subnormal temperature—R G H

La fonction THYROÏDIENNE et la procréation Favreau (M.), J de méd de Bordeaux, 1922, 3, 87-89

This article is a review of some of the pertinent data mostly taken from French sources. These conclusions are reached. There is often sterility in cases of confirmed exophthalmic goiter, but to a lesser degree when the syndrome is evasive. Hyperthyroidism sometimes causes gestation to be more difficult, sometimes has no effect upon it, sometimes makes it easier or, rarely, aggravates it. The course of the puerperium is always physiological. Nursing usually has a good influence on the disease. The offspring might have a glandular syndrome, tetany or changes in the bony structures—R G H₁

Relations between typhoid fever and THYROID (Ueber die Beziehungen zwischen Typhus und Schilddrüse) Fleckseder (R.), Wien klin Wchnschr, 1922, 35, 34

The author often observed that typhoid fever was much milder in patients with than without an enlarged thyroid. In Graves' disease, however, the prognosis of typhoid fever seems to be bad. A thyroiditis or strumitis after typhoid fever is not at all rare. No other infectious disease so often produces an inflammation of the thyroid. During typhoid fever the distribution of the blood in the body is abnormal, and it is well known that the thyroid is extremely sensitive to a want of oxygen. It is also generally accepted that the thyroid plays an important part in metabolism. Therefore, if the relation between typhoid infection and the thyroid is due to the defective circulation of this organ, we may also expect to find that in patients with parenchymatous goiters the metabolism is diminished instead of increased during typhoid fever. This is true, such patients lose only very little weight during typhoid. It is remarkable that the patient with goiter and typhoid fever generally shows a defective formation of agglutinins. The author has tried the effect of thyroid preparations in typhoid fever but without result—J K

(THYROID) A case of Graves' disease made worse by radiation of the OVARIES (Ein Fall von Morbus Basedowi, verschlechtert durch Röntgenbestrahlung der Ovarien) Fleischner (F.), Wien med Wchnschr (Wien), 1920, 70, 2008-2010

Fleischner, of the First Medical Clinic in Vienna, reports a case of Graves' disease in a woman aged 41, with a cutaneous edema

of the lower part of the body resembling scleroderma, in whom irradiation of the ovaries was followed by amenorrhoea and aggravation of the general condition. He alludes to two other cases on record in which x-ray treatment had a similar effect—*Med Sci*, 5, 302

(**THYROID**) A case of retrosternal goitre (*Osservazioni sopra un caso di gozzo retrosternale*) Franchini (F), *Pathologica (Genova)*, 1922, 14, 121-122

The author reports a case of retrosternal goitre pressing upon the heart and large vessels. The pulsations transmitted by the vessels as well as the x-ray picture had led to the diagnosis of aortic aneurism. The heart was pushed down into the left hypochondrium and the corresponding diaphragm was convex towards the abdomen. Other details as regards circulatory adjustments are described—G V

Experiences with **THYROIDECTOMY** and ligation of the thyroid artery in depancreatized dogs. Friedman (G A) & Gottesman (J), *Proc Soc Exper Biol & Med (N Y)*, 1921, 18, 281-282

Three dogs were subjected to pancreatectomy and the relation of thyroid deficiency to the resulting glycemia was studied. In the first case fractional extirpation of the pancreas resulted in marked glycosuria. After thyroid extirpation, leaving the parathyroids intact, the urine became sugar free and remained so until death, despite liberal mixed diet and 150 gm glucose by stomach tube. In the second case complete pancreatectomy resulted in glycosuria and blood sugar of 250 mgs. Following ligation of both superior and inferior thyroid arteries, the urine became sugar free and blood sugar dropped gradually to 50 mgm in 4 days. A third case resembled the second except that ligation of the thyroid arteries on one side only failed to reduce the sugar and that the dog died of tetany—R G H

(**THYROID**) Diagnosis, prognosis and treatment of Graves' disease (*Diagnose, Prognose und Behandlung der Basedowschen Krankheit*) Holmgren (J), *Wien klin Wchnschr*, 1922, 35, 47

For the diagnosis of Graves' disease palpation of the thyroid is highly important (whether Graves' disease exists without goiter is unknown, if so, it is extremely rare). A technic for the palpation of the thyroid is given. The second symptom is tachycardia, which is not influenced by drugs. Exophthalmos is not always present in mild cases. A specific action of antithyroidin has never been observed by the author. Sodium phosphate as recommended by Kocher and the injection of sodium nucleinate often give good results—T K

Hen feathering induced in male fowls by feeding THYROID Horn-
ing (B) & Torrey (H), Anat Record (Phila), 1922, 23, 132

When fed thyroid daily, in doses increasing with their weight, from the age of three weeks, male Rhode Island Red chicks developed plumage of the female type, although males of this breed do not ordinarily pass through a juvenile stage characterized by plumage of the female type. The plumage of capons, usually ultra-male, is not affected by thyroid feeding. Castrated females which typically develop male plumage are similarly unaffected. The primary effect of the thyroid feeding seems to be to increase the activity of the "luteal" interstitial tissue of the testis. The end result is a hen feathered male resembling in all essential characteristics of plumage the hen feathered males of the Seabright and Campine breeds—Author's abst

The relation of the THYROID to certain stages of metamorphosis in frog larvae Hoskins (Margaret M), Anat Record (Phila), 1922, 23, 21

The thyroid anlage was taken from its normal position and grafted into the tails of the larvae. When the animals had reached their maximum size and had well developed legs, the tails containing the thyroid grafts were cut off. With few exceptions these thyroidless animals completed metamorphosis. Examination of sections has been made to eliminate all cases in which thyroids regenerated in the normal position, and it was found that although a large percentage of regeneration was present, a number of the frogs were actually thyroidless. It is therefore evident that the thyroid is not directly necessary for the later stages of metamorphosis—Author's abst

Formation of anti-bodies in THYROIDECTOMIZED animals (Formation d'anticorps chez les animaux éthyroïdes) Houssay (B A) & Sordelli (A), Compt rend Soc de biol (Paris), 1921, 85, 1220

The omission of some lines in their note of July 21, 1921 (See Endocrin, 1922, 6, 353, has obscured the sense. The anti-sheep serum furnished by thyroidectomized rabbits has a titer for hemolysins higher than the controls. The titer for agglutinins is also higher in the thyroidectomized rabbit and horse, than in the controls. The statement as to antitoxins remains the same—T C B

Some observations on goiter based on a routine study of 800 consecutive THYROID patients Jones (E G), J M Ass Georgia (Atlanta), 1921, 10, 821-824

Four per cent of the subjects were negroes, the rest white. Only 8 per cent were males, but the percentage of the toxic type was greater among men, owing to the high incidence of non-toxic

goitres in girls Twenty-five per cent had one or more relatives with history of goitre About half had goitre in the immediate family No relation between water supply and goitre could be recognized No significant correlation between pelvic disorders and goitre could be found In the exophthalmic group the goitre was first noticed at an average age of 27.8 years More than 50 per cent occurred before 25 Twenty per cent occurred before 18, and an additional 7 per cent are thought to have appeared at puberty, disappeared, and reappeared at ages ranging from 26 to 49 Thirteen per cent of this class thought the symptoms antedated the enlarged thyroid, while 35 per cent thought the goiter and symptoms appeared simultaneously, so that only about 50 per cent noticed the goitre before the symptoms In the class of patients with toxic symptoms without exophthalmos the interval between the appearance of the goitre and the appearance of the symptoms is considerably longer than is the same interval in exophthalmic patients Three cases of carcinoma were included in the series Temporary post-operative disturbance of the voice was not infrequently seen, and a few cases of aphonia persisted from 4 to 12 weeks A maximum amount of thyroid tissue was commonly removed at one or more operations Recurrences have not been a significant feature Blood pressure ranged from 90 to 240 mm Hg in various cases Jones believes that hypertension is merely incidental, not symptomatic of the disease The mortality in toxic goitre was less than 1 per cent In the whole operative series it was 1.4 per cent The best record was 155 operations between deaths The mortality during the last year was 0.8 per cent

—R G H

The influence of **THYROID** preparations on the blood picture and especially on eosinophilic cells Kamikozawa (Y) Cent J of Med (Japanese), No 349, Jap Med World, 1921, 1, 18-19

The administration of thyroid preparations in 6 cases of bronchial asthma caused a decrease in eosinophils in 7-10 days In some cases there was an initial rise The decrease lasted very long in some cases while in others it stopped very soon The asthmatic and pulmonary symptoms improve with a decrease in the eosinophils The improvement may not be radical The results of the action of adrenaline, pilocarpine atropine, etc., on the eosinophilic cell count agree with those of Bertelli, Falta and Schweeger that the drugs that increased the tension of the sympathetic nerves caused an increase of polynuclear cells and a decrease of eosinophils, while those that increase the tension of the vagal nerves produced an increase of mononuclear and eosinophilic cells —Chem Abst 10, 286

Secretory phenomena in pathological human **THYROIDS** Key (J A), Anat Record (Phila), 1922, 23, 23

In hyperactive thyroids the mitochondria and secretion antecedents are increased and can be studied In a series of 50 pathological thyroids a study has been made of the mitochondria and secretion granules and vacuoles —W J A

(**THYROID**) Prophylaxis of endemic goiter (Prophylaxe des endemischen Kropfes) Klinger (R), Wien klin Wchnschr, 1922, 35, 35-37

In regions where goiter is endemic it ought to be the duty of the government to give to the children in schools tablets of an iodine compound These tablets ought also to be given as much as possible to the adults and event to patients for years after strumectomy to prevent recurrence —J K

(**THYROID**) Struma maligna König, München med Wchnschr, 1921, 68, 1669

The author describes an operation during which the tumor, the trachea, the jugular vein and the lymph glands had to be removed —J K

(**THYROID**) Myxedema with pituitary enlargement (Myxédème moyen et réaction hypophysaire) Mauriquand (M) & Barre, Presse méd (Par), 1922, 30, 86

Report a child 22 months old, presenting features of typical myxedema and hydrocephalus The tongue is hypertrophic and interferes with deglutition, the thymus is normal, the testicles are somewhat large Urinalysis gave negative findings The x-ray reveals an enlarged sella with effaced clinoid processes, denoting an indubitable hypertrophy of the hypophysis Family and personal history were negative Attention is called to the fact that an increasing number of this type of cases is being reported and to the diagnostic value of enlargement or deformity of the sella —G L

(**THYROID**) Foreign cells in human goiters (Ueber Korperfremde Zellgebilde im menschlichen Kropf) Merk (L), Mitt a d Grenzgeb d Med u Chir (Jena), 1922, 34, 554-566

The author sometimes found remarkable cells in goiters Sometimes he found a large number of spores They can be found by making a very small hole in a follicle and sucking out some liquid with a capillary pipet If this liquid has a tobacco-like color it contains spores Often the wall of a follicle contains brown or yellow grains in which there are enormous quantities of spores Another cell, that is not so rare in goiters, is called by the author "rust-cell" because of its color Cells of this sort are frequently

found in conglomerates which may be seen with the naked eye. The cells have a round or egg-shaped form and they contain a large granular nucleus. They stain with iodine or Sudan III. The protoplasm generally contains rust-colored granules. A third type, that is, however, very rarely found in goiters, is the "egg-like" cell. Cells of this sort look somewhat like eggs of helminths or cysts of protozoa. Merk has seen them only three times. Though the author is not sure, he believes that the three cells are stages in the development of a protozoon.—J K

(THYROID) Exophthalmos and limitation of the eye-movements of Graves's disease. Moore (R F), *Lancet* (Lond), 1920, ii, 701

There has always been doubt as to the cause of exophthalmos in Graves' disease. Moore describes the three common theories: (1) That it is due to irritation of the sympathetic nerve, (2) to engorgement of the orbit with blood, (3) to an increase of the orbital fat. He says it is still stated that the exophthalmos disappears after death, which would support the first two theories. In a case which he saw after death the exophthalmos was still present. He reports a case in which the exophthalmos was so marked that it was necessary to undertake some procedure to save the eyes. The lids of the right eye could not be sutured. He therefore made an incision through the inferior conjunctival fornix and was able to remove a large quantity of fat, after which the lids were easily approximated. He noticed that, in addition to the excess of fat, the fat itself was very edematous, as were also the inferior, internal, and external recti muscles. He deduces from this that the usual cause of the exophthalmos is an increase of fat and the limitation of movement is due partly to the pushing forward of the eye and partly to the edema of the muscles.—*Med Sci*, 5, 326

Anti-THYROID serum. Nagaoke (H), *J Japan Microbiol Soc*, 15, No 5, *Jap Med World*, 1921, 1, 20

Goat immune serum prepared by repeated injection of the antigen of dog thyroid precipitated the emulsion of dog thyroid. This immune serum lowered the blood pressure of the rabbit. Intravenous injection in a puppy caused dyspnea, increased heart rate and spasm of the limbs. At autopsy the thyroid, liver, kidneys and spleen were found to be hyperemic. There was dilation of the blood vessels of the thyroid and an increase of the colloidal substance in the vascular net-work, also slight degeneration in the liver and kidneys.—*Chem Abst*, 16, 287

(THYROID) Patients treated with radium (*Inferme trattati col radium*). Pascale (G), *Gazz d osp* (Milano), 1921, 42, 1096

This article describes a patient with an enormous goiter, with tachycardia and exophthalmos cured by the application of radium
—J K

THYROID and Graves' disease (Schilddrüse und Basedowsche Krankheit) Rautmann (H), Med Klin (Berl & Wien), 1921, 17, 645-649, 688-690

Rautmann, of the Freiburg University Medical Clinic, regards the tachycardia, exophthalmos, and morbid excitability of the whole nervous system, and increase of metabolism, as due to over-activity of the thyroid. Although he is convinced that the thyroid plays a leading part in the pathogenesis, he admits that Graves' disease may sometimes be caused by an abnormal stimulation of the nervous system, the over-action of the thyroid being secondary. Moreover, owing to the intimate relationship of the ductless glands with one another, he thinks it possible that involvement of another endocrine organ such as the thymus may be the primary cause of the development of Graves' disease—Med Sci, 5, 301

(**THYROID**) Graves' disease and the war, a critical review of the emotional origin of the exophthalmic goitre (*La maladie de Basedow et la guerre critique de l'origine émotive du goitre exophtalmique*) Roussy (G) & Cornil (L), Presse méd (Par), 1920, 28, 753-756

In a critical review of the emotional origin of Graves' disease, Roussy and Cornil state that only seven or eight cases which have been published in France, and a few in other countries, can be regarded as supporting this theory. In none of the cases could they find that a sudden emotion had given rise to the disease. Several other neurologists, such as Barré, Crouzon, Lépine, and Lhermitte, who had been in charge of special centres during the war, had also declared that they had never seen a typical case of exophthalmic goitre following a war condition. Roussy and Cornil therefore regard it as a mistake to insist on making emotion responsible for a syndrome in which the emotional state represents the effect rather than the cause—Med Sci, 5, 301

(**THYROID**) The occurrence of retrobulbar neuritis in Graves' disease (*Über einen Fall von Neuritis nervi optici retrobulbaris als Frühsymptom der Basedowschen Krankheit*) Sattler (H), Wien med Wchnschr (Wien), 1921, 71, 1084-1088

According to Sattler, of Leipzig, the occurrence of retrobulbar neuritis in Graves' disease is very rare, and has not hitherto been described as an initial symptom. He records a case of Graves' disease in which a diminution of visual acuity was the first thing that induced the patient to seek medical advice. All other possible causes of the neuritis could be excluded, and resection of the thy-

roid simultaneously benefited the retrobulbar neuritis, exophthalmos, and other symptoms of Graves' disease. A few other cases have been reported in which on improvement of Graves' disease the optic neuritis subsided. There are also cases on record of misuse of thyroid tablets being followed by retrobulbar neuritis, and finally Sattler found that experimental administration of thyroid tablets to animals produced a disease of the optic nerve resembling toxic amblyopia—*Med Sci*, 5, 302

(**THYROID**) *Struma maligna* Schaedel, *Deutsche med Wchnschr* (Berl), 1922, 48, 209-210

Reported elsewhere—J K

(**THYROID**) Graves' disease (*La critica clinica del Basedow*) Schiassi (B), *Policlin* (Roma), 1920, 27 (Sez chir), 126-145, *Abst Med Sc*, 4, 341-342

It is estimated that the medical treatment of exophthalmic goitre results in cure in 60 per cent of the cases. Resort to operative measures, when this treatment fails, is contemplated with some reserve in view of the possible occurrence of such accidents as tetany, hemorrhage, and collapse, which are liable to follow the operation. From a study of his own cases Schiassi considers that these accidents may be avoided if suitable precautions are taken and he recommends that whenever a fair trial of medical treatment is not followed by decided improvement, operation should be considered. The only operation that he regards as satisfactory is partial excision of the gland. He has used the methods of bilateral excision of the cervical sympathetic and ligation of the thyroid artery in several cases, but has found that in nearly half recurrence happened. On the other hand, in 37 cases of partial excision immediate cure resulted, and in 28 of these the operation has been performed sufficiently long to justify the inference of a permanent cure. He attributes these good results partly to a careful technique, but attaches particular importance to the choice of suitable cases and the proper preparation and after-treatment of the patients. In selecting cases for operation it is indispensable to ascertain the condition of the myocardium by repeated examination. The degree of regularity in the cardiac rhythm and in the tension of the pulse, and the amount of dilation both of auricles and ventricles are the points to which attention should be chiefly directed, fluoroscopy is valuable. In Graves' disease the circulatory symptoms are often transitory, when permanent, myocarditis is suggested, hence operation should not be undertaken. Other contra-indications are serious gastric crises, profuse and protracted diarrhoea, and chronic diffuse edema. The author also attaches much importance to signs of any considerable degree of paresis of the parasympathetic system, persistent paresis of the ocular

muscles (ptosis, strabismus), marked tachycardia persisting during sleep, and general asthenia, uninfluenced by medical treatment. In presence of these symptoms death during or after the operation would be a likely event. Schiassi considers that rest in bed for eight or ten weeks preceding operation is indispensable, and isolation desirable, to insure perfect physical and mental tranquillity. Small doses of morphia and veronal should be given every evening, and during the day time *canabis indica*, *belladonna*, and *valerian* have been found useful. As the time for operation approaches it is desirable to retain an abundance of liquid in the body, and hence the usual pre-operative purgative is omitted, water is given freely by mouth, and during the last two days, also, Locke's solution per rectum. Local anesthesia should be avoided, since it does not preclude the possibility of some mental excitement on the part of the patient. Skillful ether anesthesia is advantageous and morphia is a useful adjuvant. The post-operative treatment is analogous to the pre-operative, and should provide complete and prolonged isolation and avoidance of emotional disturbance. The action of the heart is usually upset for the first few days and morphia may be given with considerable freedom. Repeated enemas of potassium bromide and of Locke's solution are also of value. Finally, the circumstances which were the determining causes of the disease should be eliminated.—R G H

(THYROID) Treatment of Graves' disease (Zur Behandlung der Basedowschen Krankheit) Schloeszmänn, *Deutsche med Wchnschr* (Berl), 1922, 48, 244

Only the disease with exophthalmos, tachycardia and goiter should be called Graves' disease. Treatment may be by internal or by surgical methods. In either case, perfect rest is very necessary. Antithyroidin may give temporary improvement only. X-ray treatment sometimes improves, sometimes aggravates the condition. Internal treatment is used in the "formes frustes" only, and in patients in whom the disease is so serious and acute that operation is impossible. In all other cases, the author recommends operation in the first six months of the disease. Removal of the thymus is not recommended.—J K

Embryology of the derivatives of the pharyngeal pouches and the THYROID gland in the lapwing [Die Entwicklungsgeschichte der Schlundtaschenderivate und der Thyreoidea beim Kiebitz (*Vanellus cristatus* Meyer)] Sicher (Lydia), *Ztschr f Anat u Entwicklungsgesch* (Berlin), 1921, 62, 233-270

Of morphological interest only.—A T R

(THYROID) Myoclonus and Graves' disease (Myoklonie und Glandula thyroidea) Simmonds (O), *Med Klin* (Berl & Wien), 1920, 16, 1113-1114

Simmonds, of Frankfort, records two cases of myoclonus in women aged 22 and 28, in whom the condition was cured by thyroid gland tablets, which were given because, in addition to the myoclonus, symptoms were present in both cases that indicated thyroid insufficiency. The theory that myoclonus is due to auto-intoxication especially affecting the thyroid is thus confirmed by these two cases—Med Sci, 5, 304-305

(THYROID) Syphilis as a cause of goiter (Syphilis van de schildklier) Smit (J H R), Nederl Tijdschr v Geneesk (Amst), 1921, 1, 156-159

Smit records two cases of toxic thyroiditis due to syphilis with all the symptoms of Graves' disease in women aged 34 and 52, respectively, who were both completely cured by a course of anti-syphilitic treatment—Med Sci, 5, 302

(THYROID) Statistical study of simple and toxic goiter at Jefferson Barracks, Mo Smith (F M), J Am M Ass (Chicago), 1919, 72, 471-472

Being itself a summary, the article is not amenable to abstracting. It should be read in the original by those interested in the statistics of goiter. The study is based upon examination of 65,507 men from 15 states—R G H

(THYROID) A study of the correlation of the basal metabolism and pulse-rate in patients with hyperthyroidism Sturgis (C C) & Tompkins (Edna H), Arch Int Med (Chicago), 1920, 26, 467-476

In a study of 496 basal metabolism determinations on 154 patients with hyperthyroidism, Sturgis and Tompkins found tachycardia of 90 or more to the minute associated with a basal metabolism of +15 per cent or more in all but 16 per cent. In 70 instances where the metabolism fell to normal there was a simultaneous fall in pulse-rate in 78 per cent to below 90. In 52 patients in whom a number of metabolism determinations were made the pulse-rate gave an accurate idea of the course of the disease as compared to the basal metabolism in 85 per cent. In a series of 107 hospital patients with various diagnoses and normal basal metabolism only 5 had a heart-rate of 90 or more to the minute. There was in general an interrelationship between the pulse-rate and metabolism when a group of individuals was considered, in other words, an extreme degree of tachycardia suggested a greatly increased metabolism, while a slight tachycardia usually indicated a slight or moderate increase. The fact that a pulse-rate below 90 per minute is seldom and below 80 per minute is rarely associated with an increase in metabolism is regarded by Sturgis and

Tompkins as of great practical importance in the recognition of a large group of nervous patients who have symptoms similar to those occurring in hyperthyroidism—Med Sci, 5, 303

Interrelation of THYROID and PITUITARY in producing metamorphosis Swingle (W W), Anat Record (Phila), 1922, 23, 41

Data given elsewhere

Experiments with necturus and axolotl THYROIDS Swingle (W W), Anat Record (Phila), 1922, 23, 100

Data elsewhere

The THYROID glands of perennibranchiate amphibians Swingle (W W), Anat Record (Phila), 1922, 23, 106

No thyroids could be found in Typhlomolge The thyroid glands of tadpoles with prolonged larval lives have a meager blood supply compared with adult urodeles—W J A

(THYROID) Incomplete Graves' disease with small tumor and metastases in the bones (Syndrome de Basedow incomplet chez une malade ayant une petite tumeur thyroïdienne avec métastases osseuses) Tixier (L) & Duval (H), Bull et mém Soc méd d hôp de Par, 1921, 3 s, 45, 874-876

A case of malignant tumor of the thyroid with metastases in the bones is reported by Tixier and Duval As is the rule in such cases, as shown by Lenormant, the picture of Graves' disease was incomplete, tachycardia and tremor being present and exophthalmos absent—Med Sci, 5, 302

The influence of THYROID and of temperature on metamorphosis of tadpoles (L'azione della nutrizione tiròidea sullo sviluppo delle larve di anfibî, sotto l'influenza di temperature varie) Terini (T), Monitore zool ital (Firenze), 1919, 30, —, —, Abst, Schweiz med Wchnschr (Basel), 1920, 50, 1102

Terini fed larvae of *Bufo vulgaris* with thyroid substance Some experiments were carried out in an incubator at 28° C and others at room temperature from 9-15° C The heat increased the reaction to thyroid feeding very noticeably, irrespective of the stage of development at which it was begun The influence of the two factors is on the whole similar Both hasten differentiation, without influencing growth The metamorphosis proceeds rapidly The larvae, however, remain small as compared with those developing under normal conditions Although the increased temperature and the thyroid feeding mutually reinforce each other the high temperature alone does not produce precipitate and unharmonious development as does thyroid feeding—R G H

The function of **THYROID** gland with special reference to the effect of variations of diet upon it. Tsuji (K), *Acta scholae med univ imp (Kioto)*, 1920, 3, 713-728

Twenty-two young rats were fed on a diet of casein 22 per cent, starch 42 per cent, cane sugar 21 per cent, lard, 12 4 per cent, salts—from incinerated rice—2 6 per cent. The materials were carefully purified. Seven rats received 2-3 cc of milk in addition. Six young rats and six adults were also fed on unpolished rice and as much minced thyroid as they would eat. It was found that rats fed on the artificial diet alone showed arrest of growth, thus confirming results of previous authors. The thyroid glands of all these animals showed some typical histological changes, chiefly atrophy, with considerable decrease in weight. The changes of the thyroids were connected with the diminished function of the glands (hypothyroidism), which, according to the author, induced a profound change in many of other organs (testes, ovaries, submaxillary gland, parotid gland, pancreas, liver and suprarenals). The changes of these organs stood in contrast to those produced by thyroid feeding (hyperthyroidism). The testes of artificial diet-fed rats showed decrease in weight and diminished spermatogenesis or degeneration of the cells contained in the seminiferous tubules. The ovaries of artificial diet-fed rats were also decreased in weight and showed the degeneration of the ova and the follicular epithelia with premature ovulation. The mucous part of submaxillary gland was affected neither by artificial diet feeding nor by thyroid feeding. The typical changes were produced first in the tubuli and next in the other alveoli of the serous part both by artificial diet feeding and by thyroid feeding, while the former caused a resting state and degenerative atrophy of the glands, the latter induced activity and hyperplasia (mitoses of cells) of the glands. It is noteworthy that similar changes were produced in the parotid gland and the pancreas both by artificial diet feeding and by thyroid feeding, indicating that these two are analogous. The parotid and the pancreas of artificial diet-fed animals presented an appearance of a resting state in light cases and atrophic changes of the alveolar cells in severe cases. Thyroid feeding caused continuous activity, hyperplasia, or hypertrophy (shown by the mitoses of cells or the increase in the weight of organ), of both glands and the appearance of vacuolation in the alveolar cells. While the hepatic cells of artificial diet-fed animals were smaller and showed an increase in the amount of granules, the thyroid feeding produced a decrease of granules with the disappearance of glycogen and the appearance of mitoses. The suprarenals of artificial diet-fed animals were decreased in weight.—R G H

(**THYROID**) The effect of iodine and iodothyron on the larvae of salamanders. IV. The role of iodine in the inhibition of **THY-**

MUS-FED salamander Uhlenhuth (E), J Gen Physiol (Balt), 1922, 4, 319-320

Larvae of *Amblystoma maculatum* cease growing at 26 days and die at about 82 days if fed on thymus in iodine-free water. The addition of one drop of M/20 inorganic iodine to the water has no effect. Growth is resumed, however, even at 80 days, if the animals are placed upon a diet of earth worms —M E C

Simple and relatively safe THYROIDECTOMY Van Hook (W), Med Rec (N Y), 1921, 100, 1072

The writer recommends thyroidectomy with preservation of small masses of the gland at the four cornua and a thin layer of parenchyma upon the undisturbed posterior layer of the capsule. Kocher's collar incision is employed. The distinctive features of his operation are as follows: (1) The preliminary, partial hemostasis which is quite simply provided by applying light artery forceps across the whole of each of the upper cornua and across the anterior portions only of the inferior cornua. If desired, suture-ligatures may replace the forceps after pressure has been maintained for a moment. With many small artery forceps at hand, the gland-tissue is then shaved off the posterior capsule from one side of the thyroid to the other, small bleeding vessels being caught by forceps. (2) Sutures are used to close the capsule remnants by partial infolding in such a manner that only a minimum of vessels need be especially ligated. But all vessels, including the superficial veins, must be definitely closed either by this suture pressure about the capsule or by direct ligature. The method is rapid, orderly and safe —Author's abst

Recent researches on the THYROID (Quelques données récentes sur le corps thyroïde) Vignes (H) & Cornil (L), Prog méd (Par), 1922, 37, 113-116

The article is a summary of some of the more recent evidence. It does not lend itself to abstracting —R G H

Endocrinology

The Bulletin of the *Association for the Study of* **Internal Secretions**

July, 1922

STUDIES ON THE PARATHYROIDS III.

TWO CASES OF COMBINED ENLARGEMENT OF THE THYMUS GLAND AND OF THE LOWER PARATHYROIDS

HILDING BERGSTRAND

STOCKHOLM, SWEDEN

CASE I SVEA INGEBORG ANDERSSON, 22 YEARS OLD

The patient was taken into Sabbatsberg Hospital on Nov 17, 1916, and discharged Jan 20, 1917. The diagnosis was *appendicitis acuta gangraenosa perforata cum peritonitide purulenta bilat*. During this stay in the hospital she stated that since her 17th year she had suffered from epilepsy. But no closer examination was made except concerning the appendicitis.

The patient was again admitted to the hospital Dec 14, 1917, and discharged Dec 19 with the diagnosis, neurasthenia. She stated that from her 17th year she had had attacks when she lost consciousness, fell down, and bit her tongue. The attacks seem generally to have come once a week, but more often if she worked hard. She had had struma for two years and for the same length of time had been troubled with difficulty in breathing as soon as she caught cold. In addition, she seems, during the two months before she entered the hospital, to have had a cough and shortness of breath when going up stairs. During this period the epileptic fits were also frequent. She knew of no hereditary tendency to nervous disorders. The clinical investigation gave very few objective findings. There were found a number of ronchi in the right lung, redness in the throat, and a

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struma of average size The patient was menstruating at the time All the reflexes were normal There was no rise in temperature, but a somewhat increased frequency of the pulse, varying between 80 and 100

The patient was admitted a third time on March 3, 1918, and died a few hours later When admitted she showed no obvious enlargement of the heart, but a rapid pulse and ronchi above both lungs When taken into the ward the patient, who did not seem especially ill, suddenly turned blue and died immediately

AUTOPSY REPORT No 87 1918

On account of the relatives' opposition no autopsy could be made before three days after death In spite of this the decomposition was slight.

The body weight was 72 kg and length, 166 cm The structure of the body was very strong The shoulders and pelvis were broad. The flesh was well developed but there was no real adiposity The general color of the skin was pale The skin showed no changes The mammae were large The teeth were normal

The sawed off part of the skull weighed 480 grams, it was not quite symmetrical The tubera frontalia and parietalia were rather thick while other parts of the cranium were thinner The juga cerebri were not especially developed All the bones of the body were hard and firm without any signs of softening

The dura was of normal thickness The soft membranes were thin, transparent and smooth The arteries were thin walled. The brain weighed 1365 gr A moderate amount of clear fluid was found in the ventricles The brain parenchyma was firm It was evidently slightly hyperemic The pineal gland weighed 100 mg and the hypophysis 800 mg

The heart weighed 280 gr The myocardium was firm, contracted and brownish red The endocardium was smooth and shining, the valves thin and membranous No changes were seen in the aorta The mucous membrane in the throat and at the base of the tongue was swollen The tonsils were enlarged, their mucous membrane, like the surrounding mucosa, was dark red The laryngeal mucous membrane was not swollen In the bronchi was a large amount of thick mucous, greyish yellow fluid The pleural sacs were empty, the lungs, free, the pleurae smooth and transparent The right lung weighed 525 and the left, 470 gm Both were fairly voluminous and rich in fluid, not contracted as usual but stretched out as if they were fixed in the position of inspiration The pressed out juice was fairly rich in blood in the back parts but clear everywhere The parenchyma was pale in the front parts and dark red in the back parts The lymphatic glands in the hilus of the lung were as large as a brown bean and pale in color No spots of any kind were found in them and no signs of obstruction in the air passages

The liver weighed 1480 gm and was dark red Its consistency was normal, as was the surface of the section The gall bladder contained dark green bile The pancreas was pale and weighed 70 gm

The mucous membrane of the stomach and intestines was cadaverously stained by blood pigment, otherwise it was normal

The peritoneum was smooth and shining all over There was no appendix The right kidney weighed 140, the left 125 gm The surface beneath the easily loosened renal capsule was smooth The cut surface was dark red and with fairly distinct markings, its consistency was firm The uterus weighed 80 gm., its musculature was somewhat diffusely hypertrophic. The right ovary weighed 10, the left, 6 gm The latter was attached to the uterus by connective tissue adhesions, which were however easily loosened There was a large corpus rubrum in the right ovary The cervix was vaginal, the vagina was normal

The spleen weighed 250 gm. Its capsule was somewhat tense, its cut surface dark brownish red with especially prominent greyish white follicles. The consistency of the parenchyma was fairly loose. The bone marrow in the diaphysis of the right femur was yellow.

The right adrenal weighed 4.50, the left, 5.75 gm. They showed the ordinary color and structure. The thyroid weighed 28.5 gm and showed a dark red, firm parenchyma. The thymus weighed 39 gm. Its parenchyma was greyish white and was very like the parenchyma in an infant. The parathyroids weighed: right upper, 25 mgm; right lower, 310 mgm; left upper, 45 mgm; and left lower, 320 mgm. The lower were firm, the upper, flaccid.



Fig 1 Thymus and parathyroids in Case I. Reduced one-half

Microscopic examination The spleen showed swelling of the sinus endothelia and the pulp cells. There were no 'centres of growth' in the follicles. There was considerable hyperemia.

Pieces of the back parts of the lungs showed in sections patches of coagulated fluid in the alveoli. There was no cellular exudation. The capillaries in these regions were considerably dilated.

The kidneys showed in relation to the patient's age an apparently increased number of sclerotic glomeruli in the most superficial layers of the cortex. Around these glomeruli was an infiltration of lymphocytes. Otherwise the vessels, glomeruli canals and interstices were normal.

The pancreas was very much altered on account of decomposition, especially the islets of Langerhans. The adrenals contrasted sharply with this, as both their medulla and cortex were completely preserved and showed the clear and apparently normal demarcation.

The thyroid showed follicles filled with hard, firm colloid which cracked when sectioned. The epithelium was cubical, there was no extension of the epithelium into the lumen and no adenomatous vegetations or cell infiltrations in the interstices.

The ovaries showed Graafian follicles in different stages of development and corpora lutea in varying stages of regression. The interstitial tissue showed no changes.

The hypophysis and epiphysis were saved for a possible later investigation.

Parathyroids The two upper parathyroids presented an appearance normal for this age. The parenchyma was compact, i e, no ingrowing of adipose cells between the follicles had yet taken place. The cells consisted of "principal cells" in different stages of secretion and exceedingly few Welsh's cells. The "principal cells" all showed, with osmic fixation, or when stained with Sudan III, the typically great content of fat. The two lower parathyroids were on the whole identical but differed sharply from the two upper. Frozen sections fixed in osmium immediately showed that the enlargement was caused by a new formation occupying the main body of the glands. This new formation had thrust aside the old tissue, which lay like a thin peel outside the new. The sharp demarcation between the new and the old tissue was due to the fact that the cells of the former were free, or practically free, from fat, while the old cells retained their normal abundance of fat (Fig 2). On the other hand, there was no capsule around the new formation. In these respects the conditions agreed with what is usually observed in new formations in the parathyroids.



Fig 2 Lower right parathyroid in Case I. The darker part indicates the old parenchyma, the lighter part, the new growth. The difference is caused by the stained fat in the older parenchyma cells and the presence of large interstitial fat cells in the older tissues. Frozen section. Sudan III Haematoxylin stain.

I may refer here to photographs in a previous article (1). No typical Welsh's cells were observed in the new formation. On the other hand, there were a number of cells that seemed to be intermediate between "principal cells" and Welsh's cells. (The reason why I consistently use the expression Welsh's cells and not eosinophilic cells is that I consider the latter expression misleading. In my opinion (2) the Welsh's cells are degenerated "principal cells" appearing

Table I

	Hasall's Corpuscles per Mg. of the Medulla										Total													
	Group																							
	Group																							
	I	II	III	IV	V	VI	VII	VIII																
Case I 21-25 years Average minimum and maximum figures (Hammar)	90 60 0 60 20 48	10 86 4 02 13 64	6 09 2 08 8 16	4 57 1 04 5 85	1 3 1 0 1 7	9 68 5 14 13 90	11 3 2 14 23 31	20 5 4 9 30 23	13 7 10 4 24 2	3 3 2 1 7 8	2 1 0 8 2 1	1 2 0 08 7 8	0 6 0 04 0 1	0 06 0 0 0 3	57 4 41 8 75 2	26 3 8 6 54 2	61 8 30 8 73 5	31 9 23 2 50 1	0 0 5 5 16 3	2 9 0 2 4 5	1 5 0 2 2 7	0 09 0 0 0 3	0 1 0 6 0 6	133 7 86 3 175 8
Case I Age 22 years Female	37 4	22 44	11 03	10 51	1 1	14 06	3 3	5 5	3 6	2 1	1 2	0 7	0 0	0 0	15 4	7 1	11 8	5 5	4 5	2 5	1 5	0 0	0 0	32 0
Case I Age 58 years Female	27 7	11 60	0 28	5 32	1 2	16 00	0 38	23 3	5 25	0 75	1 48	0 203	0 0	0 0	40 36	0 84	50 0	11 4	21 3	3 2	0 44	0 0	0 0	88 08

	The Absolute Number of the Hasall's Corpuscles										Incubated Hasall's Corpuscles				
	Group										Sum	The Relation Between Group I and II	The Absolute Number		
	Group												Pro Mg. of the Parenchyma	Pro Mg. of the Medulla	The Absolute Number
	I	II	III	IV	V	VI	VII	VIII							
Case I 21-25 years Average minimum and maximum figures (Hammar)	120 310 18 402 254 272	282 481 110 052 370 102	145 903 97 284 182 277	41 340 25 543 71 030	13 347 920 25 284	0 061 920 15 652	448 0 1 168	024 0 3 504	0 0 0	0 0 0	611 418 204 510 823 973	1 2 3 1 1 3 1 6 0	1 3 3 0 8 6	3 0 0 0 17 8	13 691 36 120 0
Case I Age 22 years Female	74 062	123 420	58 344	47 124	20 028	15 708	0	0	0	345 576	1 1 6	0	0	0	0
Case I Age 58 years Female	17 745	27 250	20 190	1 060	204	0	0	0	0	07 097	1 1 5 1 1 0 1 2 1	3 2 0 0 6 9	7 1 0 0 14 1	3 051 0 12 903	
Case II 50 years Female	4 408	270 180	60 000	113 100	17 168	2 354	0	0	0	408 110	1 61 3	0	0	0	0

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normally as a phenomenon of age, while in the parathyroids there are also other "eosinophile" cells forming principal cells filled with secretion and in full activity. Even the old tissue had in this case no Welsh's cells, nor did colloid occur anywhere.

Thymus This gland was examined in the ordinary way in microscopic sections and also quantitatively analyzed by Hammar's paper method (3). The latter part of the investigation was carried out at Hammar's own laboratory. Before the investigation 1.5 gm of connective tissue was set aside. A renewed weighing after this preparation showed the weight of the thymus as only 35.5 gm. According to Hammar's formula, $39 \times 35.5 = 37.0$, the real weight of the thymus would then be 37.4 gm.

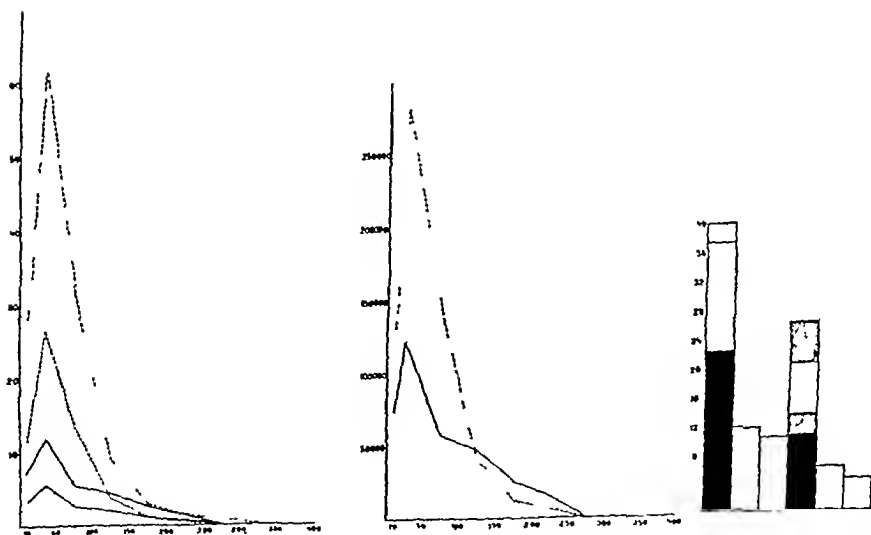


Fig 3 Shows the relation between cortex, medulla and interstitial tissue in Case I. Cross sections of the glands magnified 3 times. Explanation of graphs in text.

The result of the investigation is shown in Table I and Fig 3. In this table are given, first, the figures for the two cases investigated here, and, second, for the sake of comparison, Hammar's averages and maximum and minimum values of the thymus in healthy persons belonging to the same age classes.

who have suddenly died from external causes. The table records the weight of the parenchyma, the cortex, the medulla, and the interstitial tissue as well as the relation between cortex and medulla. The number of Hassall's corpuscles per mg parenchyma and per mg medulla and the absolute number of such formations in the whole organ are included. The Hassall's corpuscles are divided into 8 groups of magnitude, including within their limits corpuscles of a diameter of 10-25 μ for group I, 25-50 μ for group II, 50-100 μ for group III, 100-150 μ for group IV, 150-200 μ for group V, 200-300 μ for group VI, 300-400 μ for group VII, 400-500 μ for group VIII. Finally, figures are given to show the relation between groups I and II and the number of calcified Hassall's corpuscles per mg parenchyma and per mg medulla and in the whole organ. The data are shown graphically in Fig 3. The left curves show the number of Hassall's corpuscles per mg of parenchyma and medulla and the right curves the absolute number of these corpuscles. The abscissae give the size of the Hassall's corpuscles and the ordinates their number per mg of parenchyma and medulla and in the whole organ. The complete lines denote the case in question, the hatched lines Hammar's average values for a corresponding age. Of the curves at the left the upper denote the Hassall's corpuscles per mg of medulla, the lower, the corresponding numbers for the parenchyma as a whole. The diagram at the right shows the weight of the organ as a whole and the weights of the different components in it. The three columns at the left in the diagram refer to the case described in this paper and indicate, from left to right, the weight of the whole thymus body, the cortex and the medulla respectively. The numbers of the ordinates denote grams. In the column that shows the weight of the organ the part of the column that gives the weight of the interstitial tissue is empty. The three columns farthest to the right show in a corresponding way Hammar's average values for a corresponding age and also the maximum values for the parenchyma and the entire weight of the organ. These latter values are shown by the hatched parts of the columns and are given so as to show how far the maximum values of the case under discussion exceed Hammar's maximum values both as to the entire organ and as to parenchyma.

Direct microscopic investigation showed a very distinct boundary between medulla and cortex. Between the lobuli was seen a fairly abundant interstitial tissue consisting mostly of fat cells. The veins running in this tissue showed no thickening of the wall. The interfollicular tissue also consisted of fat cells. These mostly projected from the interlobular fat tissue in the form of wide sweeps, narrowing as they approached the medulla. In many places, however, this was not the case, but the interfollicular tissue seemed compressed and had only very narrow communication outwards, even this was sometimes absent, so that the fat cells were situated in rows between the follicles quite embedded in the parenchyma.

CASE 2 FRU MARIA BACK, 58 YEARS OF AGE

The patient was admitted to the hospital on Sept 8, 1919, and died Oct 10, the diagnosis being *vitium organicum cordis et haemorrhagia haemisphaeri sinistri cerebri*. The patient stated that a week before admission she had had an attack of unconsciousness with simultaneous paralysis of the left side. The day before admission she had had a similar attack. Investigation at the hospital showed that the patient had hemiplegia, without aphasia, on the left side. The blood pressure was 100-110 mm Hg. The heart showed some enlargement and a presystolic sound was heard. There were traces of albumin in the urine. The Wassermann reaction in the blood was negative. The temperature was afebrile. The pulse rate was about 70. The patient's condition remained unchanged until Oct 10, when she suddenly became unconscious, dying within 3 to 4 minutes.

AUTOPSY REPORT NO 358 1919

The body length was 156 cm, the build, powerful. The weight and musculature were only slightly reduced. In general, the skin was pale in color. There was no edema.

The bones of the skull were of normal thickness and firmness. There was no osteoporosis. The brain membranes were normal. There was no arteriosclerosis in the basal brain arteries. No thrombi or emboli were visible. On the right side, in the lateral nucleus lenticularis was a red soft spot, extending out into the capsula interna and occupying in its entirety a space about the size of a walnut. The cerebellar parenchyma was otherwise of normal consistency and color.

The pericardium was smooth and shiny. Due to a right sided myocardial hypertrophy the heart was somewhat large, weighing 300 gm. The musculature was pale brownish red and of firm consistency. There were no scars or discolored spots in it. The segments of the mitral valve were thickened and fused so that the mitral orifice could transmit only one finger. On the atrial side of one of the segments was seen the place of attachment of a loosened thrombus in the form of a rough surface the size of a hemp seed.

The lungs held air in all parts and their parenchyma was soft. The fluid that was pressed out was clear everywhere. The liver was of normal size, greyish red in color. The stomach and intestines were normal. The kidneys were firm and dark red with a distinctly demarcated cortex. The parenchyma

showed no patches except a number of fibrous scars from healed infarcts. No fresh infarcts were observed. The spleen weighed 130 gm. The lymphatic glands were apparently not enlarged.

The ovaries showed senile atrophy. The thyroid gland weighed 30 gm. All four parathyroids were found and weighed as follows: right upper, 40, right lower, 120, left upper, 40, left lower, 370 mg. The thymus was greyish red, large and 90 gm. in weight. The adrenals and hypophysis were preserved at the autopsy but were not weighed, which fixed the former weighed 5+5.5 gm., the latter, 695 mg.

P. A. D. *Encephalomalacia hemorrhagica capsulae internae dextrae et Endocarditis chronica cum stenose valvulae mitralis*

Microscopic examination Because of the hasty post mortem examination a smaller number of organs was taken for microscopic examination in this case than in the preceding. Unfortunately, among the endocrine organs thus omitted from microscopic examination were the ovaries. The thyroid gland and adrenals appeared normal. The only thing of note is that in this case, too, the adrenals showed no signs of cadaverous softening. A transverse section of a rib showed no pathological changes. On the other hand, the kidneys showed, besides the above mentioned scars, acute degeneration in the canals, the epithelium of which was swollen and in the lumen of which was a mass, coagulated in meshes. The same thing was observed in the cavity of Bowman's capsule. The parenchyma showed no fatty degeneration and Weigert's fibrin stain was also negative. The capillaries in the glomeruli were filled with blood. There was no cell infiltration and no changes in the vessels. It was difficult to find hyalinized glomeruli.

Parathyroids The two upper parathyroids showed quite normal conditions with a moderate growth of fat between the lobuli and a moderate number of Welsh's cells. The appearance of the newly formed parenchyma and its relation to the old showed exactly the same conditions as in the preceding case. It is therefore unnecessary to repeat the description.

Thymus The thymus was investigated in the same way as in the preceding case. The figures for the numerical investigation are given in Table I and the table is made clearer by the curves and diagrams given in Fig. 4. For the explanation of these see the description under Case I. The boundary between medulla and cortex was also very sharp in this case. The interstitial material consisted of adipose tissue. A large number of veins in this showed an extreme thickening of the adventitia. The interfollicular tissue was of the same sort as in the preceding case and showed the same curious arrangement, but it was somewhat less distinct. It may be mentioned that the sharp boundary between medulla and cortex at this age does not occur regularly in normal cases. Hammar's material from which the figures are taken, consists of six cases, in three of which there was no distinct difference between the medulla and cortex. This is the cause of the lack of agreement apparently seen in the table between the figures for parenchyma, medulla and cortex.

DISCUSSION

Of the two cases described the first is undoubtedly the more interesting. According to the patient's statement she had suffered from frequent attacks of epilepsy. During her stay in the hospital, certainly very brief, in December, 1917, no such attacks could, however, be observed and the clinical diagnosis was neurasthenia. Nor were any epileptic fits observed during a two months' stay in the hospital a year earlier. It is thus impossible to decide whether the patient had really suffered from epilepsy. The symptoms at her death do not support the assumption.

tion that she died of epilepsy. The statement in the journal as to the high frequency of the pulse and the enlarged thyroid gland of course suggest exophthalmic goiter. This would also

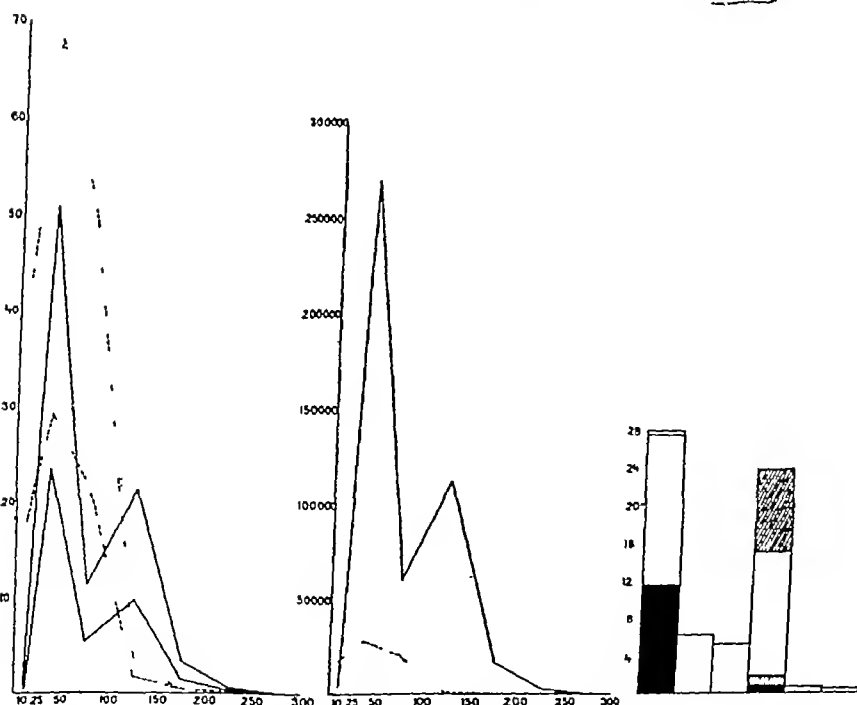


Fig. 4 Shows the relation between cortex, medulla and interstitial tissue in Case II. Cross sections of the glands magnified 3 times. Explanation of graphs in text.

explain the manner of death. The post-mortem and the histological investigations show, however, that there was no enlargement of the thyroid gland and that this gland did not show the

features usual in exophthalmic goiter. Nor was there any enlargement of the heart. There was certainly thymus hyperplasia, but, as we shall see, it was of quite a different type from that which Hammar (4) found to be characteristic of Graves' disease. This diagnosis must, then, be rejected. As a matter of fact, neither the records of the illness nor the autopsy give any satisfactory explanation of the cause of death. The redness of the throat, the swollen tonsils, the contents of the bronchi, and the acute swollen spleen certainly indicate that, when the patient was admitted to the hospital, she was suffering from an infection in the upper air passages, but these findings do not give any explanation of the sudden death. It is noteworthy that the patient stated that during the two last years she had suffered from trouble in breathing as soon as she caught cold, especially if these statements are connected with the fact that at autopsy the lungs were found fixed in the position of inspiration. This leads one to think that the extremely enlarged thymus might have exerted compression on the trachea and the main bronchi. On further reflection, however, one must admit that such an assumption is very improbable, for the thymus is so soft and plastic an organ that it is rather improbable that it should be able to exert any considerable deforming pressure on such resistant structures as the trachea and bronchi in an adult. Nor were the contents in the bronchi of such a quantity and nature that the curious position of the lungs could be explained as due to bronchial obstruction. The only possibility left is the idea that the agonal inspirations caused the expansion of the lungs. No changes in the microscopic picture due to the expansion of the lungs can be traced.

The data as a whole indicate that the most plausible explanation of the course of the illness and the post-mortem findings is some sort of endocrine disturbance. The large thymus gland quite naturally suggests what is called status thymico-lymphaticus. But, in my opinion, this term is as yet so little fixed that I shall not enter upon any discussion of the case from this point of view, but merely relate the actual conditions and the more obvious reflections to which they give rise.

First, as to the parathyroid enlargement, we must decide upon its nature. It is often difficult or impossible to distinguish

between an autonomous growth, i e, a real tumor, and a reactive hyperplasia. This applies not least to the parathyroids, as I have had opportunity to show in a previous communication. In the present case, everything indicates an autonomous growth. It is true that two glands are enlarged, but bilateral neoplasia are not unknown in the paired human organs. Moreover, the new formation is distinctly circumscribed and unicentric, all of which strongly supports the idea of a tumor. On the other hand, the histological character of the cells of the new formation affords less evidence. The absence of fat in the cells and the lack of Welsh's cells and colloid are typical both of autonomous and reactive growth. These characteristics show only that we are concerned with young cells, which is also indicated by the fact that the parathyroids of infants have exactly this character. If we suppose that we are concerned here with an autonomous growth, which seems rather certain, and that the enlargement of the parathyroids and the hyperplasia of the thymus have really something to do with each other, then the latter must be a result of the former, because it can be supposed that hyperplasia of the thymus may possibly give rise to a reactive enlargement of the parathyroids, but not to an autonomous one. That a connection of cause and effect is really present, can of course not be proved by only two cases, but on the other hand we are so accustomed to changes in the endocrine organs being connected with one another that we certainly have some right to make an assumption of this sort. It is true that in previous cases of parathyroid enlargement I have observed, no hyperplasia of the thymus was found, nor have I been able to find any statement to this effect in the literature, but I must confess that I had not previously submitted this gland to examination according to Hammar's method and this is necessary if we are to get a reliable view as to its condition.

I pass now to an analysis of the thymus. Here it is of the greatest interest to make a comparison with the discoveries made by Hammar in his investigation of hyperplastic thymus glands in exophthalmic goiter.

In the case described we have a very extreme increase both of medulla and of cortex. The figures are more than double the average weight for a corresponding age and are considerably

above the maximum values. The weights of the parenchyma may thus without hesitation be described as above normal. We must note that Hammar's normal values are based on material derived from healthy persons who died suddenly from external causes. The deviations with regard to the weight of the thymus that others report all tend towards values less than those given by Hammar. It is thus certain that we have here a supranormal parenchyma value. The increase in the cortex and medulla was parallel. The value for the medulla is comparatively high and consequently we have a low index, which is now, however, below the limit for the normal. Here we find the first deviation from the hyperplastic exophthalmic thymus in which, in typical cases without secondary accidental involution, the cortex has the greatest share in the increase and consequently, we get a high index. Hassall's corpuscles show, for the four lowest orders of magnitude, subnormal values per mg parenchyma and medulla. The deviation is very great. If we turn to the absolute values we find that they lie within the normal limits and in such a way that the lower orders of magnitude approach the lower limit while the higher orders reach and even exceed the upper limit. Thus the Hassall's corpuscles have not followed the increase of the other components of the parenchyma in the thymus. But further, to judge from the low values for the small Hassall corpuscles, it even looks as if there was a deficient new formation of such corpuscles. Quite opposite conditions prevail in exophthalmic goiter, for there, according to Hammar, we get supranormal total values, supranormal or at least high values per mg of parenchyma and medulla respectively, and a surplus in the lower orders of magnitude.

In his above mentioned work on exophthalmic goiter Hammar discusses in detail the question as to whether a hyperplasia or a possible subinvolution can be considered as being present here with regard to the supranormal glands. The weight of the parenchyma gives no certain fixed points nor do the absolute numbers of the Hassall corpuscles, for they are within the normal values for the thymus at puberty, of which we have not sufficient knowledge. The occurrence of sclerotic veins in the interstitial tissue and the arrangement of the interfollicular fat cells is considered by Hammar to indicate that we are concerned

with hyperplasia in what was previously an involution thymus. He does not finally reject, however, the possibility of a subinvolution. The same is true in this case. The very high parenchyma value does not exceed Hammar's maximum value for the age 16-20, which for the entire parenchyma is 22 gm. Nor is the amount of interstitial tissue sufficient to indicate a previous greater development in an involution organ. On the other hand, this tissue is so prominent that it is impossible that we have a persistent juvenile thymus. When I use the expression thymus hyperplasia above in reference to the case described here this is thus only an expression of my subjective view. A "thymus persistens" may be present. In this case it offers the peculiarity that not all the components of the parenchyma "persist." The Hassall's corpuscles are of course, as we have seen, quite reduced to values that are very considerably subnormal for this age. The veins of the interstitial tissue do not show the above mentioned sclerotic feature the most prominent microscopic characteristic of which is an extreme thickening of the adventitia. On the other hand one sees clearly the curious arrangement of the interfollicular fat cells, for these lie, as we have seen, in rows either enclosed in the parenchyma or with a very narrow communication with the interlobular tissue. The interlobular adipose tissue normally projects on a broad basis in between the follicles. As in the thymus in exophthalmic goiter, so here, too, we get an impression that the interfollicular adipose tissue has been squeezed together by the growing follicles.

Of the cases of supranormal thymus glands investigated by Hammar and his school the case mentioned here resembles most one that Hammar (5) has mentioned in a work on the so-called thymic death. This was a case of a 23 year old man who, after having been quite healthy, jumped out of his bed one morning and fell dead. The post-mortem showed bronchopneumonia in the earliest stage and the diagnosis was "lymphatismus." Both my case and Hammar's, on the other hand, undeniably show a certain similarity to a number of cases described in literature under the diagnosis, status thymico-lymphaticus. In the above mentioned case there was a supra normal parenchyma value of 16.51 gm, the relation between

cortex and medulla gave a low index of 0.9, the Hassall corpuscles showed low absolute values and low values per mg of parenchyma, though this applied only to the lowest groups of size. Hammar draws from this the conclusion that the Hassall corpuscles have decreased their reformation while they continue to grow. The top of the curve was displaced to group III.

SUMMARY

In a 22 year old woman with a curious and unexplained record of illness, who suddenly died, there was found, besides slight signs of an infection in the air passages, two parathyroid glands showing extreme enlargement, due most probably to autonomous growth. The thymus showed a similar extreme enlargement caused by a supranormal amount of parenchyma and interstitial tissue quite different from that of the juvenile type. It was probably a hyperplastic, not a subinvolted thymus of puberty. It differed from the hyperplastic thymus in exophthalmic goiter in that only the values for cortex and medulla were supranormal, while the total number of Hassall's corpuscles was considerably lower than normal for a corresponding age. There was probably not only a relative but also an absolute decrease in the new formations of Hassall's corpuscles. There was a striking similarity to the thymus in a case of "lymphatismus" described by Hammar. The case affords further support of Hammar's theory that the different components in the thymic parenchyma may independently vary in amount.

In a 58 year old woman, who had an attack of hemiplegia and died about a month later from a second attack, the two lower parathyroids showed enlargement due in all probability to autonomous tumor growth. The thymus gland was markedly enlarged with a parenchyma value more than 10 times the normal. As in the preceding cases the thymus was taken to be hyperplastic, not subinvolted. All the parenchyma components were increased, cortex and medulla to the same degree, but the Hassall's corpuscles to a smaller extent. The values for the Hassall's corpuscles per mg parenchyma and medulla, respectively, were therefore low. In spite of the differences between them, the cases fall in a sharply defined group in which the hyperplastic thymus differs from that of exophthalmic goiter.

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SOME OBSERVATIONS ON THE NATURE AND DIAGNOSTIC SIGNIFICANCE OF THE WHITE LINE OF SERGENT ("LIGNE BLANCHE SURRENALE")

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LITERATURE

"La ligne blanche surrénale"—the white line of adenal insufficiency was first described by Sergent (1) in 1903. Since that date considerable literature of a very conflicting nature has sprung up regarding it. During the period that has elapsed, important changes have been made in our views of the physiology of the adrenal glands and many of the older conceptions of the functions of these organs have been profoundly modified. In the light of these facts, it was thought that a systematic study of the nature and significance of the white line of Sergent would be of interest.

If the skin of the abdomen in a suitable individual be lightly stroked with some round smooth object, it is found that after a definite latent period a white line appears which gradually increases in intensity and definiteness. It persists for a minute or longer and then slowly fades. This phenomenon was first noted quite accidentally in a patient in whom a diagnosis of meningeal irritation had been made. The involvement of the adrenals was not suspected at the time, and was revealed only by the post-mortem examination which showed that the glands were almost completely destroyed by caseating tuberculous masses. On subsequent investigation Sergent found the white line constantly present in subjects showing symptoms of adenal insufficiency.

According to Sergent cases of this condition may be classified into the following groups

- A Pure adrenal insufficiency
 - 1 Fulminating (with sudden death)
 - 2 Acute ("syndrome Sergeant-Bernard")
 - 3 Sub-acute
 - 4 Mild ("petite insuffisance")
- B Adrenal insufficiency with involvement of the pericapsular nerve plexuses
 - 1 Addison's disease

The fulminating cases are of medico-legal interest only as the patient is suddenly struck down dead. Upon a post mortem examination the only lesion found is destruction of the adrenal bodies. Addison's disease, when typically present, is a well defined condition which may be recognized with some certainty. The other varieties mentioned give rise to very diverse clinical appearances as will be seen from a consideration of the symptoms.

The cardinal symptoms are arterial hypotension and asthenia of varying degrees. Digestive disturbances, such as vomiting, diarrhea, constipation, or severe abdominal pain, giving rise to a diagnosis of some acute abdominal catastrophe may be superadded. Excitement, convulsions, encephalopathy, abnormal eye signs or coma may be present. Syncope, small pulse, tachycardia and other symptoms suggestive of circulatory disorders may be found. The clinical picture being thus so ill-defined, certain recognition of these cases becomes almost impossible in the absence of some pathognomonic sign. Thus, Sergeant contends he has supplied, in the white line. He affirms that cases that would otherwise never have been suspected as suffering from disturbed adrenal function may by this means be readily recognized. He does not claim that the white line is present in every case of adrenal insufficiency, and admits that it may occasionally occur when the glands are functioning normally. Similar reservations must, however, be made in the case of the rose-spots in typhoid fever, but it is argued that in neither case does this detract from the diagnostic importance of the sign.

Sergeant believes that adrenal insufficiency may be present as a complication in many other diseases (especially the acute infectious fevers), although no anatomical lesion of the glands can be discovered. It is suggested that the secretion, though

normally formed, is neutralized by the toxins of these diseases, and is thus unable to fulfil its normal function in the body

In a recent publication (2) Sergent has collected most of the evidence in support of his interpretation of the significance of the white line. It is said to be a constant accompaniment of arterial hypotension, though rarely it may be elicited when the systolic pressure is higher than normal. The diastolic pressure in these latter cases is stated to be low, so that the pulse pressure is greater than usual.

All cases of Addison's disease in which the cardinal symptoms of adrenal insufficiency, asthenia and low blood pressure are present, show the white line. When melanoderma is the principal feature, the white line may not be found. The lesion is then regarded as mainly periglandular and not involving the adrenal bodies themselves.

In the various types of adrenal insufficiency, medication with whole gland or adrenin alone is said to improve the general condition. The blood pressure may rise, and then the white line can no longer be produced.

The white line is regarded as dependent on a condition of hypoadrenia. The "tonus" theory of the function of the adrenal bodies is adopted, namely, that the arterial blood pressure is maintained at its normal level by the constant secretion of the active principle of the glands. Should this be diminished in amount, hypotension results and the peripheral arterioles tend to be more dilated than usual. Light mechanical stimulation brings about constriction of these vessels, the blood supply of the corresponding area of skin is diminished and a white line is thus produced. The validity of this hypothesis will be considered later.

A number of authors have described experiences which support the views of Sergent. Among these may be mentioned Sicard (3), Bossuet (4), Siredy and Tinel (5), Paisseau and Lemaire (6), Betchov and Demole (7), and Babonneix (8).

Masselongo (9) has reported a systematic investigation on 400 patients. The white line was found in only 30 cases of this series. Of these, 22 were suffering from typhoid fever. Many cases with definite lesions of the adrenal glands did not show the white line. He thinks the sign is of considerable prognostic

value, as all the patients in whom the white line was present, died

L Bernard (10) obtained the white line in 31 out of 79 patients in a general hospital, i e, almost as many patients showed the white line as did not

As adrenal insufficiency is known to be not a very common condition, this finding appears to cast doubt on Sergent's assertions. The sign is intermittent in appearance and does not seem to bear any relation to the condition of the patient. Bernard concludes that the "ligne blanche" is not a sign of hypotension nor of adrenal insufficiency.

Masary (11) in a number of communications has come to a similar conclusion. He regards the white line simply as a "trouble vaso-moteur banal."

Timme (12) finds the white line present in the first and second stages of the pluriglandular syndrome described by him. He does not regard its association with adrenal insufficiency as proved. He states, however, that it invariably accompanies low blood pressure. It disappears quickly after a hypodermic injection of adrenin. Emotional disturbances make the eliciting of the sign impossible. In cases of Timme's syndrome, the white line can no longer be produced when the patients improve.

Professor Swale Vincent has kindly allowed me to mention that some few years ago the late Sir William Osler mentioned to him that he considered our knowledge of the cutaneous vaso-motor reflexes unsatisfactory, and thought that they would repay re-examination. He suggested that it would be well to examine very carefully the evidence for the diagnostic value of the "ligne blanche surrénale."

PERSONAL OBSERVATIONS

It will be seen from the account of the literature that, though many observations have been made on subjects suffering from various morbid conditions, no thorough investigations are recorded on the normal subject*. In the absence of satisfactory control experiments, it is difficult to decide on the value which may be attached to the mass of clinical evidence which has already been accumulated.

* See final paragraph

The subjects of the present research were a number of healthy young medical students attending the course of Physiology in this Medical School. The technique adopted was as follows. After the clinical history had been taken, the subject was placed in the recumbent position for some minutes with the abdomen free, but lightly covered. A geometrical figure was then lightly traced on the skin of the abdomen with the round smooth end of a fountain pen. The directions of Sergent were closely followed. No pressure was exerted, and no scratching occurred. The response was then noted.

The blood pressure was taken in all cases in the recumbent position with the arm at heart level. The instrument employed was an aneroid type of sphygmomanometer (Tycos). The auscultatory method of Korotkoff was used. The diastolic end point was taken as Point V of Swann, i.e., the disappearance of all sound. If 14 mm be added to the readings given, the diastolic pressure is obtained in terms of the higher end point.

It soon became obvious, contrary to what had been expected, that many normal individuals gave a white line in response to light stroking. The white line, when present, varied widely in intensity and definiteness, and also depended, in a manner to be described, on the strength of stimulus employed.

Sergent (13) has given certain criteria of the "true" ligne blanche surrénale. This line appears after a definite latent period, it lasts for one minute or longer, it appears gradually, slowly intensifies and finally fades, it is not preceded, accompanied or followed by any red lines whatever. No response was accepted as positive unless it showed all the features detailed.

For purposes of description, it was thought advisable to define two main grades of response.

1. Marked (++) in which the line was perfectly definite, and could be seen with great ease. The edges were clear cut.
2. Definite (+) in which the line could not be seen so easily, or was brought out only on carefully shading the skin. The outline was not so sharp.

A third group in which the response was negative was also recognized. It comprised those individuals in whom the white

line was preceded or accompanied by a red line, in whom the white line was too indistinct to be quite certain about, or in whom no response at all could be observed

One hundred individuals were examined and the results obtained are summarized in the accompanying table

TABLE I

WHITE LINE

	Marked	Definite	Negative
Av systolic pressure	130 mm	129 mm	132 mm
Av diastolic pressure	69 mm	70 mm	72 mm
Av pulse pressure	61 mm	59 mm	60 mm
Percentage of cases	27	39	34

As will be seen from the last line of the table, no fewer than 66 per cent of the normal subjects examined showed the white line. Sergeant, however, insists that the true "*ligne blanche surrénale*" must have an "*intensité vive*". It is a matter of some difficulty to decide in any individual case whether this requirement is fulfilled, but even if all the cases described as "white line, definite" are excluded, there still remain 27 per cent of normal persons who give a response identical with that which is alleged to be indicative of adrenal insufficiency.

The average blood pressure, both systolic and diastolic, in the three groups corresponds very closely to one another. The average systolic blood pressure in Group I (white line, marked) was 130 mm, the range being from 150 mm to 112 mm, in Group II (white line, definite) 129 mm, the highest being 146 mm * and the lowest 108 mm. In Group III (white line, negative), the average was 132 mm, the pressures lying between 158 and 112 mm.

The diastolic pressure figures are equally striking. In Group I, the average was 69 mm and the range 90-60 mm, in Group II, 70 mm and 80-55 mm, in Group III, 72 mm and 90-65 mm.

There does not, therefore, appear to be any relation between the height of the blood pressure and the intensity of the white line. Many individuals with high systolic or high diastolic

* In one neurotic subject it was 175 mm

pressures gave very marked reactions, while some with low pressures gave negative responses

Some observations of Ravaut and Kronulitsky (14) confirm the view expressed above, though the authors themselves interpret their results differently. In 75 normal subjects the white line was definitely present in 27, a red line being obtained in the other 48 cases. The blood pressure was not taken. The authors consider the evidence, anatomical, clinical and therapeutic, conclusively in favor of the diagnostic importance of the white line, and consequently regard the 27 cases as instances of mild suprarenal insufficiency. In view of the results obtained in the present investigation, it would appear safer to argue that the white line is a phenomenon having no pathological significance, rather than assume that over one-third of apparently normal individuals are suffering from an admittedly rare condition like adrenal insufficiency.

OTHER "WHITE LINES"

A careful examination of the literature shows that a number of physiological responses have been described which bear a close resemblance to the phenomenon of Sergent. It will be useful to refer to them in this place and discuss their significance.

As long ago as 1875 Vulpian (15) described a white line which could be seen in normal individuals after lightly stroking any region of the skin "*à condition que l'excitation ne soit pas très énergétique*". He quotes Baumler (16) (1873) to the effect that this line can be obtained in the first stage of "*typhus exanthématique*" and that "*la facilité avec laquelle on provoque alors la production de ces tramées blanches le porte à penser que l'excitation des artères serait plutôt augmentée que diminuée dans ces conditions morbides*".

A "*ligne blanche physiologique*" was described by Duval (17) in 1885. The technique employed was not, however, identical with that of Sergent. The latter admits that this "*ligne blanche*" can be obtained in normal subjects, especially on the back of the hand and on the cheek, but maintains that it is *never* to be seen on the skin of the abdomen. It is only the pathological white line which is found in this region. The results of the present research do not support these statements of Sergent.

Hallion and Laignel-Lavastine (18) describe a "tache blanche" which is produced in normal individuals by pressing heavily on the dorsal surface of an interosseous space until the skin is completely blanched. They timed the duration of the pallor and employed it as a test of the activity of the circulation. It bears no relation to the line of Sergeant.

L. R. Muller (19) has made an extensive study of the various types of dermatographism and their significance. He has obtained a white line (dermographia alba) on superficial stroking in many normal young individuals, especially those with dark skins. After the age of 45, this response is less commonly obtained. The line was best marked in patients with certain nervous diseases, i.e., tabes, disseminated sclerosis, transverse myelitis (on the paralyzed side of the body). He appears to be unaware of the work of Sergeant, but his technique is identical in all essential features. He thinks it questionable if this "dermographia alba" has any diagnostic significance.

Cotton, Slade and Lewis (20) have repeated and confirmed Muller's observations. The subjects in their case were soldiers in a military hospital who were suffering from disordered action of the heart.

Reference may be made at this point to the work of Tracy (21). This observer, from an examination of a large number of individuals, claims that the normal reaction of the skin to a mechanical stimulus is a brief vasodilation, followed by a more prolonged vasoconstriction. In some subjects one of the two components of the reaction was absent. It is argued that these differences depend on variations in the hormone content of the blood. A double innervation of the blood vessels of the skin from the sympathetic and parasympathetic is assumed. The vasodilation is supposed to be due to activation of the parasympathetic fibres by the "Hormone X" of Eppinger and Hess ("autonym"), while the vasoconstriction results from stimulation of the sympathetic by adrenalin*. If both components of the reaction are present, both hormones are assumed to be present in the blood. If the vasodilation component alone is present, Hormone X or its analogues are in excess in the

* It will be noted that Sergeant regarded a vasoconstriction response as indicative of lack of adrenin while Tracy produces the same reaction by injecting adrenin.

blood or the hormone adrenalin (or pituitrin with similar action) is in insufficient amount to activate the sympathetic nerve-endings in the blood vessels tested. If the vasoconstriction component alone is given, the reverse condition is present.

It is also stated that the vaso-constriction part of the response can be made to reappear in subjects in whom it was previously absent by injecting adrenin. It is supposed that the sympathetic nerve endings are thus sensitized and therefore respond more readily to the mechanical stimulus.

No attention was paid in this investigation to the strength of the stimulus employed. I am unable to confirm Tracy's observations, and in any case it is very improbable that they can bear the interpretation he places on them. It must be stated that most of the theoretical assumptions made by him are entirely unsupported by any authentic evidence.*

The white line of Baumlér, Vulpian and Sergent, the dermographia alba of Muller and the white tache of Lewis appear to be the same phenomenon, one of which is present quite commonly in normal, healthy persons. Contrary to the views of Sergent, one must conclude that the white line has no pathognomonic significance, though it is of interest to enquire more deeply into its exact nature and mode of production.

THE BLOOD VESSELS INVOLVED

It has already been noted that Sergent regarded the "white line" as an arteriole phenomenon. He believed that the mechanical stimulus produced constriction of the previously dilated arterioles, with the result that blanching of the skin was effected. Considerable evidence may however be adduced against this hypothesis.

Characteristically, the white line is limited to the area of skin stimulated and is quite sharply outlined. Muller (19) points out that this would not be the case if the blanching were due to constriction of arterioles. Each arteriole supplies an irregular area of skin and the local anemia resulting from its contraction would similarly be irregular in outline and not follow strictly the line of the stroke.

*Krogh (J. Physiol. 1920 53, 417) is extremely skeptical on the question of the supply of the capillaries by the autonomic nervous system. For a criticism of 'Hormone X' see Swale Vincent, Endocrinol. 1917, 1, 459.

The chief features of the white line can be readily explained if local constriction of the capillaries themselves is assumed

The white line can be obtained almost as readily on the skin of the forearm as on the abdomen. If the arm be raised to the horizontal and the pressure in an armlet is rapidly run up to 70-80 mm above the blood pressure of the subject (i.e., to about 200 mm Hg), it is found, as pointed out by Cotton, Slade and Lewis (20), that the white line can still be obtained and that its time relations remain unchanged. The same holds true even if an interval of ten minutes is allowed to elapse after applying the armlet

If the circulation is normal, blocking an arteriole empties the corresponding capillaries, because the blood previously contained within them flows on into the veins. The effect of compressing the arm in this experiment has been, however, to slow down or stop completely the flow in the vessels below the block and produce a stagnant circulation. In such a system, constriction of the *arterioles* would drive blood out of them into the capillaries and dilate them still further, as their contents could not pass on in the normal way, owing to the obstruction to the natural outflow from the veins. The blanching of the skin must therefore be due to the contraction of the *capillary* wall, which actively drives the blood out into the neighboring veins

If a painful stimulus, such as a pin prick, be applied to the skin, a flush results, which can readily be shown to be an arteriole phenomenon. The flush spreads a variable distance from the area stimulated, is mottled in color from alternating islets of hyperemia and normal skin, and the edge is crenated, as would be expected from the manner in which an arteriole is distributed to the skin. The color is red throughout and does not tend to become purple from oxygen deficiency, proving that rapid flow of blood is occurring and not the stagnation which is typical of filled capillaries. If, over such an area of flushing, a line of light pressure be drawn, a white line appears which replaces the erythema over an area strictly limited to the zone stimulated. As pointed out by Lewis (20), we have here the characteristic line of capillary constriction, superimposed on an irregular hyperemia due to dilatation of arterioles

It may thus be concluded that the white line is due to local emptying of the capillaries as a result of active contraction of some elements in their walls, and is quite independent of the condition of the arterioles

FUNCTIONS OF THE CAPILLARIES

It must be admitted that this view is not in accord with orthodox teaching, which hitherto has assigned to the capillaries a purely passive part in the circulation. Recent research, physiological and clinical, seems to show that these older conceptions must be seriously modified.

Krogh (22) in a series of papers has confirmed and extended the older work of Stricker (23), Steinach and Kahn (23) and Roy and Graham-Brown (23). He has made many observations on the frog to show that the reactions of the capillaries can be independent of the simultaneous reactions of the arterioles and are always practically independent of the arterial pressure. The capillaries belonging to the same arteriole may change in diameter in opposite directions. A drop of urethane solution may dilate the capillaries to a diameter of 50 μ while the parent arteriole is so narrowed that the red corpuscles can just be squeezed through one by one. Dale and Richards (24), working with histamine, obtained a fall of blood pressure when the arterioles were contracted. They could explain their results only by assuming that histamine acted directly on the capillaries and produced this active dilatation.

Rouget (25) has described branched cells arranged outside the capillaries which he considers to be the contractile elements. His results have been confirmed by Mayer (26).

Many observations on the human subject have been made at the Tubigen Clinic. By means of the capillaroscope (Hantkapillarmikroskop of Muller-Weiss) (27) direct inspection can be made of the capillaries in man. Attention is directed chiefly to the skin at the root of the nail where the capillaries do not run vertically as elsewhere, but horizontally. The results obtained by this means are in full agreement with the conclusions of the previous workers mentioned*. In the present state of knowledge, the burden of proof appears to be, as Sir Thomas

* This work has been repeated and extended in this laboratory. The results will be published elsewhere.

Lewis (20) remarks, with those who deny any powers of active contraction to the capillaries

RELATION OF RESPONSE TO STRENGTH OF STIMULUS

In many of the subjects, the relation of the response to the strength of the skin stimulus was investigated. When a definite white line was obtained on very superficial stroking, gradually increasing the strength of stimulation produced the following results. The line, which at first was quite distinct, with clear cut edges, became wider and more indefinite in outline, then a vague whiteness or no response at all was obtained. The next stage was a central pink tint, leading on to a definite red line which was often flanked by a white line on either side. Using the criteria discussed earlier, this red line can be shown to be due to capillary dilatation. Heavier stimulation, giving rise to actual pain, produced the arterial flush already described.

When the white line was not obtained, heavier stroking at first produced no response. On further increasing the strength of stimulation, a red line, not accompanied by white lines, resulted.

The following stages may thus be recognized in the normal vascular responses of the skin

- 1 Capillary constriction (white line)
- 2 No visible response
- 3 Capillary dilatation (red line)
- 4 Arterial dilatation (flush)

In a proportion of subjects, the first effect is not obtained. The red line and flush, on the other hand, are constantly present.

With all grades of stimuli, the *arterial* response of the skin appears to be vasodilatation. The *capillaries*, however, respond differently to weak and strong stimuli, a weak stimulus producing constriction, a strong stimulus, dilatation. The central red line of the red and white reaction, mentioned above, is thus due to the heavy stimulus over the line of the stroke, the bordering white lines resulting from the weaker stimulus where only slight stretching of skin is occurring. An analogy may be drawn to the arterial responses following stimulation of sensory nerves. Vincent and his co-workers (28) have shown that a weak stimulus produces a fall of blood pressure (vasodilation) while a strong stimulus results in a rise (vasoconstriction).

A POSSIBLE NERVOUS MECHANISM

It is improbable that the capillary reflexes are carried out through the central nervous system, because of the accurate way in which the reaction is limited to the area stroked. Muller believes that they are due to direct stimulation of the capillary wall—heavy stroking paralyzing the contractile elements with consequent dilatation, a lighter stroke producing contraction. Krogh (29), from his experiments in the frog, agrees that they are not true reflexes because they are unaffected by section of the nerves to the part. The response to local stimulation is, however, abolished on the application of cocaine, and he is therefore inclined to the view that they are axon reflexes. The sensory nerves divide to provide the capillaries (and arteries) with vasodilator fibres and to supply sensory nerve endings which are capable of responding readily to mechanical stimuli. Other nerves and nerve endings (with an even lower threshold value) may be responsible for capillary constriction. In subjects not giving the white line, the two opposing effects would appear to neutralize one another, until a certain grade of stimulation is attained. It should be noted, however, that Langley (30) does not regard the nerve supply of the capillaries as definitely proved.

THE SYNDROME OF ADRENAL INSUFFICIENCY

Modern experimental work has shown that the tonus theory of adrenal function must be abandoned. The evidence will be found fully discussed in the papers of Swale Vincent (31) and Stewart (32). Sargent himself in a recent communication acknowledges that the normal blood pressure is not maintained by adrenin, and presumably he would be prepared to modify his original explanation of the mechanism of the production of the white line. It has been shown above that the white line is a capillary, not an arteriole, phenomenon, and there is no available proof that adrenin has any action on the capillaries. The investigation on 100 healthy men demonstrated that the line is a physiological occurrence. This view is supported by the work of the other authors who have been quoted.

Since the foregoing was written my attention has been drawn to a paper by Kay and Brock (33), who have investigated the clinical significance of the white line. They agree that the

response bears no relation to adrenal gland activity. They find it frequently present in normal subjects (especially young adults), and it bears no relation to the blood pressure. It can be made to appear in the face of an injection of adrenalin given subcutaneously. These authors do not discuss the exact physiological mechanism of the response but appear to regard with favor Tracy's theory that it is a manifestation of sympathetico-tonia.

The position of the syndrome of adrenal insufficiency must therefore be reconsidered.

If the adrenals are completely extirpated in an animal, death results after a short period. The symptoms observed agree fairly closely with those noted in the human subject in whom complete destruction of the glands has actually occurred. If, however, a small portion of the glands be retained in the experimental animal, no ill effects whatever seem to result. The conception of *mild* suprarenal insufficiency thus receives little support from the physiological side. The human post mortem evidence is likewise too meagre to place this condition on a firm pathological basis. Diagnosis of these cases has been based on the insecure foundation of tests like the white line or the response to medication with suprarenal products. It is suggestive that equally effective cures are claimed for adrenin alone as for extracts of the whole gland. It must be remembered, too, that the symptoms of adrenal insufficiency would be those arising from a disturbance of *all* the functions of the glands, in most of the clinical records, however, there is an attempt to correlate the symptoms with the supposed functions of the medulla only.

It would appear from the foregoing that it is premature to attempt to recognize clinically a condition of mild suprarenal insufficiency until our knowledge of the part played by the adrenals in the normal body economy is considerably extended.

SUMMARY

- 1 The white line of Sergent is described and the literature of the subject is reviewed.

- 2 It is shown by an investigation of 100 healthy individuals that the white line is a phenomenon occurring in a large proportion of normal subjects and is without pathological significance.

3 A number of analogous physiological responses are described

4 The white line is not related to adrienal insufficiency nor to abnormally low systolic or diastolic pressure

5 The white line is produced by local emptying of the capillaries due to the active contraction of some elements in their walls, and is quite independent of the condition of the arterioles

6 A nervous mechanism of the nature of an axon reflex may be involved

7 The bearing of this investigation on the clinical recognition of adrenal insufficiency is discussed

I must thank Professor Swale Vincent for his kindly encouragement and advice throughout this investigation

The expenses of this research have been partially defrayed by a Government grant made through the Royal Society

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Table I "Ligne blanche" Marked (++)

SUBJECT	AGE	BLOOD PRESSURE			WHITE LINE		Clinical History and Present Condition
		Systolic mm	Diastolic mm	Pulse Pressure mm	Latent Period, Seconds	Duration, Minutes	
H M J	18	136	75	61	25	2	Good health
F J T F	23	136	90	46	15	2	Good health
E V S	19	140	65	75	15	2	Good health
F E L	19	130	65	65	15	2½	Good health
D A W	19	124	730	794	20	2	Good health
W R S P	20	125	65	60	15	2	Had 'orthostatic albumuria'
J A W	23	133	75	58	15	2	Good health
W G C G	20	128	70	56	10	2½	Good health
F G	19	118	80	38	10	2	In hospital 7 years ago for 'septic condition' Now quite well
S S	18	150	85	65	12	2	Good health
D H	21	125	80	45	10	2	Good health
H B S	20	144	70	74	15	1½	Septic tonsils.
C E B	19	118	80	38	25	3	Good health
A M M	22	125	65	60	20	—	Operation for glands in neck
D P G	19	130	60	70	20	—	Good health.
A L B	17	140	—	—	10	3	Good health.
P B J	20	132	72	60	12	1½	Good health
J W S	24	122	72	50	—	—	Good health
D C	24	128	65	63	15	1½	Good health
R H F	20	138	65	73	15	2½	Good health
C R P	22	136	60	76	10	1	Good health
R W E	20	142	60	82	15	1½	'Strained heart'
E W P	21	112	60	52	10	1½	Good health
J R	26	128	70	58	12	1¼	Good health
P B S	28	126	75	51	10	2	Malaria
J V D	29	120	70	50	12	1½	Good health
S W	23	118	75	43	10	1¼	Good health
Average		130	69	61			

Percentage of Cases, 27

Table II "Lagne blanche" definite (+)

SUBJECT	Age	BLOOD PRESSURE			Clinical History and Present Condition
		Systolic	Diastolic	Pulse	
T A B	18	132	80	52	Good health
W H G	19	132	55	77	Good health
Z R.	22	108	80	28	Good health
A L H	24	130	65	65	Good health
A D B	20	126	85	41	Good health
K S S	21	136	80	56	Appendicitis 1915 Irritable heart
A T G	25	114	85	29	Hist of syst murmur at apex Now nor
F E T	22	128	65	63	Good health
L B	24	132	80	52	Good health
J R. T	21	136	70	66	Good health
P R. P	21	138	70	68	Good health
D S D	19	128	65	63	Good health
G W A.	22	142	70	72	Neurasthenia
A. W	21	122	60	62	Good health
E J A.	23	122	65	57	Good health
D R. S	21	138	65	63	Good health
W G	25	132	75	57	Good health
D J H	22	132	70	62	Good health
L R.	18	136	70	66	Good health
H W G	23	122	70	52	Good health
W L B	21	118	64	54	Nephritis at 2
H I D	22	142	70	72	Good health
E E B	18	130	80	50	Good health
H L P	27	108	65	43	Good health
S S B	23	116	70	46	Good health
J F	21	140	70	70	Good health
W F	22	128	70	58	Good health.
S W	22	125	60	65	Good health
M R. S	24	146	70	76	Good health
F R L	17	121	65	56	Good health
M B W	25	134	70	64	Good health
H D P	22	122	80	42	Good health
G H T	23	136	66	71	Good health
W M B	24	138	70	68	Good health
C A B	26	126	70	56	Good health
T E E	25	122	70	52	Pneumonia 3 years ago
A P M	26	124	60	64	Good health
G V G	25	175	65	115	Tachycardia, pulse 130 neurotic, sweats
D E B	26	126	75	51	Good health
Average		129	70	59	
Percentage of Cases, 39					

Table III

"Ligne blanche" negative

SUBJECT	AGE	BLOOD PRESSURE			Clinical History and Present Condition
		Systolo	Diastolo	Pulse	
E A D	19	118	70	48	Good health
E J S	21	128	90	38	Good health
F D M H	22	138	80	58	Good health
G S	21	136	75	61	Good health
A G S	20	130	80	50	Good health
S W A	25	120	70	56	Good health
C G U C	18	128	70	58	Good health
J S R J	23	146	70	76	Good health
H H	25	128	65	63	Emphysema "
C A M	23	112	65	47	Good health
E D T	26	128	65	63	Good health
R J N C	20	125	70	55	Good health
J D R M	22	138	65	73	Good health
J B	23	135	65	70	Good health
W G D	28	142	75	67	Good health
M B	23	153	80	78	Good health
P R P	20	125	70	55	Good health
E O L	23	122	80	42	Good health
S G S	25	128	65	63	Good health
H G L F	24	116	65	51	Good health
G S S	20	114	65	49	Good health
C F	22	148	70	78	Good health
J W	20	126	70	56	Good health
P J M	22	146	75	71	Good health
D B M	26	146	85	61	Good health
L E M	24	142	70	72	Good health
F H A	26	148	80	68	Good health
D E T	40	132	70	62	Good health
L H R	29	124	70	54	Good health
H H J	23	126	65	61	Good health
F W C	21	126	80	46	Good health
A T F	23	128	80	48	Good health
A F D	23	142	65	77	Wound of kidney Large abdominal scar
Average		132	72	60	

Percentage of Cases 34

THE RELATION OF THE ADRENALS TO MUSCULAR ACTIVITY *

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That the adrenals bear some direct relation to muscular activity has been known for many years. One of the earliest recognized symptoms of adrenal insufficiency was muscular asthenia. This is undoubtedly the most characteristic symptom. In Addison's disease and in experimental insufficiency the loss of muscular power is very striking. Individuals previously quite strong become weak and easily fatigued.

After the discovery of epinephrin it was shown that this substance could benefit fatigued muscle (1). This suggested the possible rôle of the adrenals in muscular exercise. No one so far as we know, however, has demonstrated that there is an increase in epinephrin output during exercise. Stewart and Rogoff (2), without attempting to show any difference in epinephrin output from exercise, did not observe any difference between the working power of normal cats and those with a large portion of the adrenal tissue removed and in some instances the remaining fragment denervated.

We have studied the influence of exercise in fifty cats by means of a treadmill (3), most of them for at least a few weeks and a smaller number for considerably more than a year. Our results point to a very definite relation between epinephrin output and muscular response.

We have used the denervated pupil as a test for epinephrin. By its means we are able to recognize increases in the epinephrin output at any stage of exercise without recourse to operative procedures. That epinephrin is responsible for dilatation of the denervated pupil during exercise has been shown by denervation of the adrenals in animals which gave the reaction, after which dilatation was abolished. We have proved that such dila-

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tation is not due to central nervous influence, by removal of the ciliary ganglion as well as the superior cervical ganglion. In the five cats in which this operation has been performed exercise in the treadmill has easily elicited dilatation of the denervated pupil. Abolition of dilatation of the pupil following complete adrenal ablation in cats with the superior cervical ganglion removed and the response of a completely denervated iris with adrenals intact, are conclusive evidence that the dilatation of a denervated pupil during exercise must be due to something from the adrenals. Epinephrin, being the only substance in the adrenals known to possess this power, must be responsible for the dilatation of a denervated pupil from exercise.

All exercise is usually accompanied by some increase in the epinephrin output. But the extent of the increase is determined by the intensity and duration of the activity. Judging from the dilatation of the denervated pupil, the epinephrin is released in gradually increasing quantities during vigorous exercise. Hard fast work will develop the maximal output much earlier than will moderate activity. Two cats were led around the room at a moderate pace, one trotted along willingly, the other slid and held back. The former performed more work and gave evidence of a small increase in the epinephrin output at 51 meters, the denervated pupil being just larger than the control. The epinephrin output was maintained at about this level for the whole period of 544 meters, there being no further increase. Upon placing the animal in the treadmill there was a further increase in the output after 57 meters had been covered. The other cat did not show an increase in the epinephrin output until it had walked more than 500 meters around the room and then it was just noticeable. Upon placing it in the mill it showed a decided increase in the epinephrin output by the time it had traveled 143 meters.

The increased epinephrin output during exercise persists for some time after cessation of work—the longer the work period, and the more intense the exercise the longer the after-secretion. An increase may persist for one or more hours in some instances after vigorous work, in others it may be only a matter of a few minutes. Once the adrenals have started to secrete additional epinephrin, it is frequently very easy, after short rest periods, to obtain a very quick rise in the output.

Typical eye reactions are shown in the accompanying figure (Fig 1)

This increase in epinephrin has an important bearing on muscular efficiency

THE RELATION OF EPINEPHRIN TO THE WORK PERFORMED

We have observed that an animal can travel faster and go farther if there is a decided increase in the epinephrin output. Moreover, spurts of fast pacing in the mill have been accom-

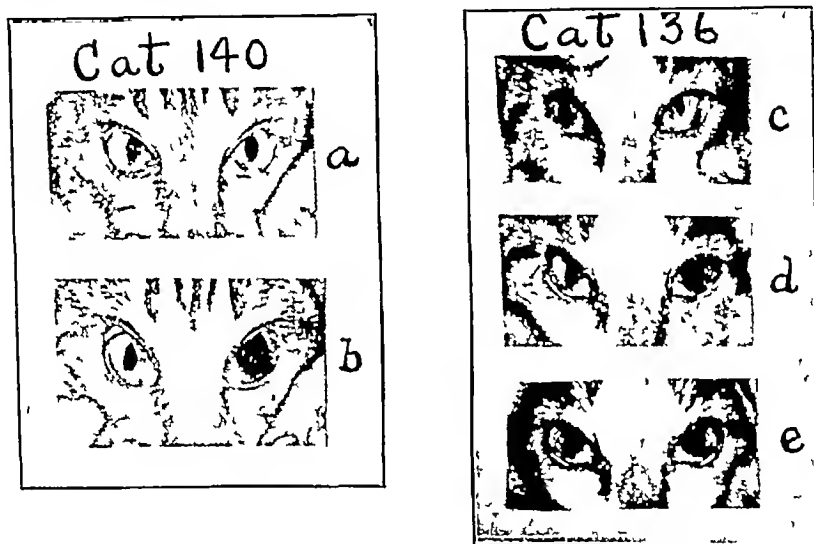


Fig 1 Dilatation of denervated pupil from exercise. Cat's left eye denervated (superior cervical ganglion removed). Cat 140: a before, b after travelling 153 meters in 3 min. Cat 136: c before, d after travelling 185 m in 5 min, e after travelling 437 m in 15 min.

panied by greater increases in epinephrin. Occasionally a perfectly normal animal will fail to show any epinephrin increase, then if the work is carried far enough it will often go into convulsions. However, the same animal is able to travel much farther when the usual increase in epinephrin is obtained (Fig 2)

Animals which are not able to increase the epinephrin output on account of denervation of the adrenals, do not work so well as normally. But if the nerves are allowed to regenerate they recover this power together with the increased epinephrin output accompanying exercise.

Adrenalin injections likewise produce a beneficial effect on the work performed. Injected intramuscularly in order to prolong the absorption, 25 cc of a 1:10,000 solution (into the muscles of the back) caused a cat which had already traveled 500 meters without showing "second wind" or increased epi-

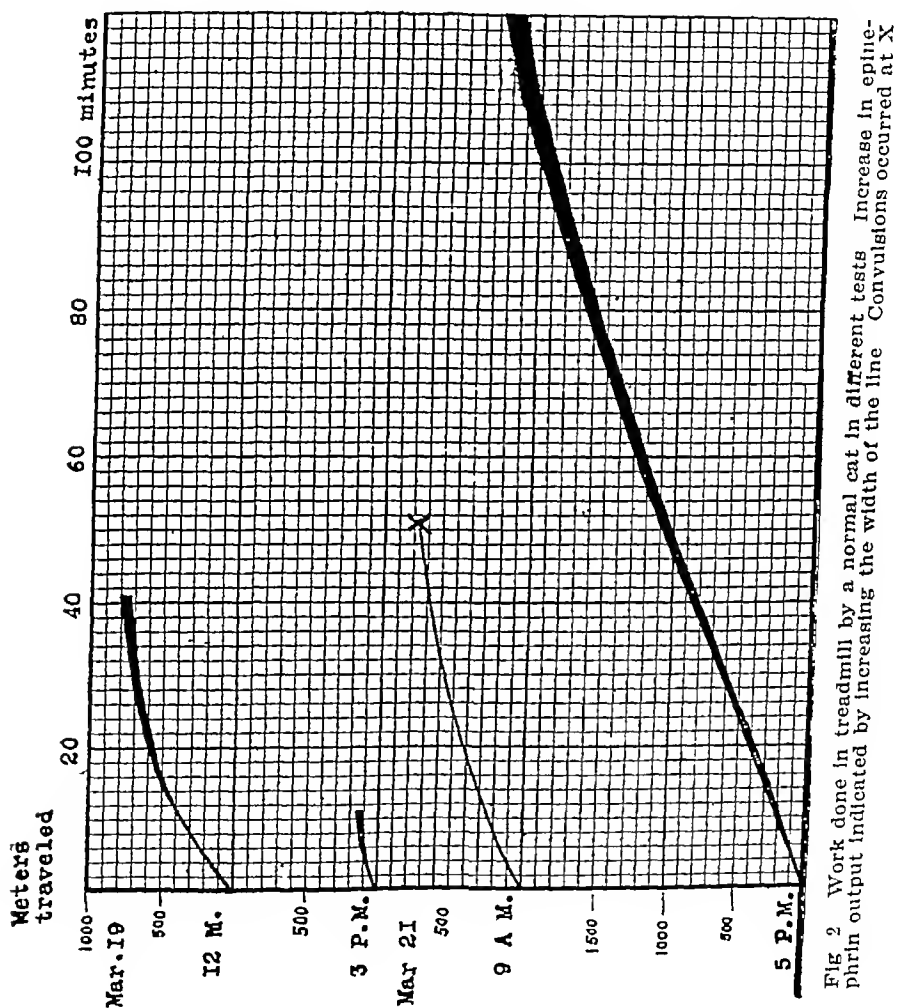


Fig. 2. Work done in treadmill by a normal cat in different tests. Increase in epinephrin output indicated by increasing the width of the line. Convulsions occurred at X.

nephin, to improve markedly in pacing and work generally during the next 500 meters. An injection of 1 cc of a 1:10,000 solution into another cat after it had worked more than 500 meters caused it to pace better than during the preceding period. The improvement continued until it was working better than ever before. Both cats possessed but a single adrenal, the nerves of which had been cut several months before. Regeneration had

taken place but was far from complete, so that a normal increase in the exercise output of epinephrin was sometimes difficult to obtain. The relation of epinephrin to working power is very well shown by the following examples

Cat A Three weeks after destruction of a part of each adrenal by cautery, testing in the treadmill for 1144 meters showed an excellent output of epinephrin (eye reaction), likewise the cat appeared to have "second wind". The cat apparently could have gone much farther. One month after removal of the right adrenal, testing in the mill showed a good increase in epinephrin, although less than in the first test, likewise the work was not so vigorous. Ten days after cauterizing the left adrenal the second time, testing in the mill showed a slight increase in epinephrin. The cat was weak but willing. On the basis of adrenal insufficiency a series of adrenalin injections were given. A total of 12.6 cc of a 1:5,000 solution was injected into the muscles in forty-seven minutes. After a portion had been injected, the cat became more active and seemed to feel better. The denervated pupil had become markedly dilated showing that epinephrin was being absorbed. However, it should be noted that it took a great deal more adrenalin to produce the required dilatation than in a cat with normal adrenals. The cat was again tested in the treadmill, working aggressively and doing very much better than in the first test. The second time it traveled 543 meters in twenty-five minutes and felt fit at the end because it jumped out of the mill and stood up. In the first test it traveled only 240 meters, the test being stopped because of the apparent weakness.

Cat B Operations, time of operations, and time of testing were identical with Cat A. The results were very similar in all tests. In the test following the second cauterization of the single remaining adrenal, the cat was obviously suffering from adrenal insufficiency because it had decreased in weight from 3.3 kgm to 2.4 kgm and appeared lethargetic. From the start of the mill, the cat appeared weak but willing. There was no evidence of an epinephrin increase. At 275 meters the cat was taken out, but it could not stand. After the injection of 4.2 cc of 1:10,000 adrenalin solution intramuscularly in the course of fifteen minutes, the cat instead of moping listlessly became active, cleaning itself. After further injections of a total of 7.5 cc of 1:5,000 adrenalin the cat was again placed in the treadmill. It appeared to have lost its former weakness, working much better than in the first test.

The improvement obtained from adrenalin injections resembles the "second wind" which has been observed in some of our cats. In fact our observations lead us to believe, with Cannon (4), that epinephrin plays an important part in the development of "second wind". At the time when our animals showed

this greater efficiency an increase in the pupil dilatation was usually noticed

The possible rôle of epinephrin in "warming up" exercise is suggested by our observations. An athlete goes through a few vigorous paces and in so doing undoubtedly forces the epinephrin output to a higher level. When he is put to the test he is able to start with a higher muscular efficiency, partly on account of the extra epinephrin already released, although of course there are other factors involved.

FATIGUE CONVULSIONS

Occasionally in normal cats and frequently in certain individuals which possess adrenals with only partially regenerated nerve fibers (the nerves having been cut some time before) convulsions will develop while the cat is working in the treadmill. The animal usually lies on its side, the whole musculature undergoing spasmodic contraction. Sometimes, it moves its feet rapidly as though it were pacing and jumping in the mill. This is accompanied by great salivation and marked dilatation of the pupil. Convulsions are frequently preceded by slight muscular twitchings. They are followed by heightened irritability in some instances and by a brief prostration in others. In no instance have there been any lasting ill effects.

Convulsions occur only in certain individuals, while in others, according to our observations, they never occur. A certain amount of work must precede these seizures. Thus for some time after removal of one adrenal and denervation of the other it is impossible to obtain convulsions because the animal will not work hard. Usually, there is no dilatation of the pupil preceding convulsions, however, in two animals only, this has occurred. One adrenal had been removed, the other adrenal had been denervated several months before in each animal. In one animal the dilatation was very poorly developed, in the other, the dilatation was marked, although not as well developed as in a normal cat. In both instances, the animals traveled much farther than was possible in the earlier period. Seven months before, convulsions would begin at from 500 to 728 meters in one cat and 476 to 1020 meters in the other. Seven months after, the first cat was seized with convulsions at 945 meters,

while the second was seized with convulsions at 1461 meters. Convulsions were less common in both animals at seven months.

The relation between dilatation of the denervated pupil and convulsions is shown by the following example. A normal animal, which had been seized by convulsions at 780 meters in the morning (no epinephrin had been secreted according to the eye reaction), traveled 2240 meters without convulsions when epinephrin was secreted. The denervated pupil dilated early in the test and continued to increase in size until it became maximal (Fig 2).

It appeared from these observations that epinephrin might prevent convulsions, therefore we tried the injection of adrenalin. Instead of decreasing the occurrence and postponing the onset, adrenalin seemed to increase the occurrence and hasten the onset. We tested four cats, three of which had previously been seized by convulsions. In all three, convulsions occurred earlier than normal. In the fourth, no convulsions developed. In every instance the animal worked hard in the treadmill before convulsions appeared. One of the cats serves as an illustration. This cat, a normal one (3.44 kgm.) had been seized by convulsions the first time it had been tested in the treadmill, but had failed to be affected in succeeding tests. Two doses of adrenalin were injected into the muscles of the back. The first was 0.5 cc of a 1:2,000 concentration. The second one, 1.5 cc of a 1:5,000 concentration, was given after the cat had traveled 400 meters. Following the second dose, the animal was "full of fight." Upon being placed in the treadmill it paced, until stopped by convulsions, 572 meters in eleven minutes. This was certainly faster and a longer continuous pacing than was ever obtained before in this cat. Moreover, before the second injection of adrenalin the cat had not paced more than three meters at a stretch.

Adrenalin, therefore, does not prevent convulsions. On the other hand we are not in position to say that epinephrin causes convulsions. Benedek (5) was able by the injection of epinephrin to cause typical seizures in seven patients out of nineteen, who were subject to epilepsy. Yet one cannot say that epinephrin is the cause of epilepsy.

SUMMARY

1 In normal animals, except in rare instances, there is an increase in the output of epinephrin accompanying exercise. This increase is greater, the more vigorous and the more prolonged the exercise.

2 The increased output of epinephrin persists for some time after the exercise ceases, the duration of the increase depending to some extent upon the amount of work performed.

3 Injections (intramuscular) of adrenalin improve the output of work in many normal cats and in cats with epinephrin deficiency.

4 An animal can go farther and travel faster when there is an increase in the epinephrin output during exercise.

5 Epinephrin may hasten the onset of convulsions due to exercise.

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A CASE OF SPONTANEOUS DISAPPEARANCE OF DIABETES

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In a previous communication (1) two cases of thyroid diabetes were reported. In these cases the glycosuria disappeared after the removal of a portion of the thyroid gland. Of the cases then reported, the second is still under observation and is still sugar free on a very liberal diet.

Since the publication of the article referred to, Friedman (2) and his co-workers have announced, and in part published, the results of animal experiments which have a very direct bearing on the question under consideration. These investigators found that if dogs were depancreatized and thus rendered diabetic, the diabetes could be rendered less severe by ligation of all of the vessels of the thyroid and that the glycosuria could be caused to disappear by the subsequent removal of that gland. This very brief summary fails to do justice to the many interesting observations made by Friedman, whose original papers should be consulted for the details.

A Russian Hebrew, female, married, aged 45 years, came under observation with the following history. A maternal aunt was said to have had diabetes. The patient recalled the usual diseases of childhood. She was married at 19 years and had five children, all alive and well. At the age of 30 she had applied for life insurance and had been rejected because sugar was found in the urine. This was her first intimation that she had diabetes. Following this she subjected herself to medical treatment, but was never sugar free, and during treatment she developed the clinical symptoms of thirst, itching and polyuria. In seven years she lost 35 pounds. At the age of 40 a stormy menopause occurred. Three years before her death, with subsidence of the menopause symptoms, repeated examinations of the urine failed to show sugar and she was able to eat candy without having glucose appear in the urine. Two years before death she noted a boggy swelling of the hands and limbs, a

general harshness of the skin, and a slowly increasing dyspnoea accompanied by attacks of vertigo. Members of her family noted mental deterioration. At that time physical examination showed a cardiac hypertrophy with a systolic murmur at the apex. The subcutaneous tissues were generally boggy and the systolic blood pressure varied from 190 to 240 mm Hg. The urine contained 3.5 gms of albumen per liter and there were numerous casts. She did not respond to treatment and died in coma of supposedly nephritic origin.



Fig 1 Section of fibrotic thyroid $\times 200$

At the autopsy several interesting lesions were found. Those not bearing directly on the subject in hand were hypertrophied cardiac muscle with relative valvular insufficiency, marked chronic interstitial nephritis, post-mortem cystic degeneration of the adrenals, fibrotic ovaries, and diffuse arteriosclerosis, most marked in the aorta.

The lesions of particular interest were found in the pancreas and thyroid. The thyroid gland (Fig 1) showed almost complete destruction of the secreting alveoli and their replace

ment by connective tissue richly infiltrated with round cells. The pancreas showed a variety of lesions. In the general region of the head there was marked fibrosis, most of the glandular elements being destroyed and only an occasional island of Langerhans persisting. In the body of the organ the outstanding histological lesion was marked hypertrophy of the islands of Langerhans, most of these structures being three to four times their usual size (Fig 2). The tail of the pancreas showed no noteworthy change.

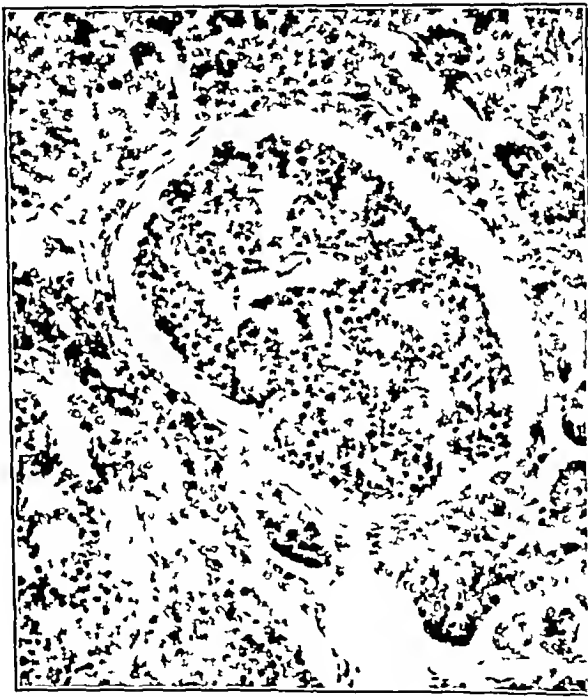


Fig 2 Section showing hypertrophy of the Islands of Langerhans $\times 200$

It is unfortunate that no detailed clinical study of this case was possible, however, conditions beyond our control prevented it. The case is, therefore, presented without further comment as a case of glycosuria accompanied by the usual clinical symptoms of diabetes, in which the glycosuria disappeared and in which, at autopsy, fibrosis of the thyroid was found accompanying which there was partial fibrosis of the glandular elements of the pancreas associated with hypertrophy of the islands of Langerhans. We have seen (3) an almost as extensive fibrosis

of the thyroid associated with a case of Addison's disease in which both adrenal glands were completely destroyed by tuberculosis, and nearly as great an hypertrophy of the islands of Langerhans in another case (carcinoma of the head of the pancreas) In the later case, as in the one here recorded, the hypertrophy was chiefly in the body of the pancreas In neither of these two cases was there any sugar in the urine With these additional cases in mind we would be reluctant to decide whether in our own case the glycosuria was initiated by thyroid overactivity and receded after pancreatic fibrosis or whether the reverse occurred

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Book Reviews

INNERE SEKRETION IHRE PHYSIOLOGISCHE GRUNDLAGEN UND
IHRE BEDEUTUNG FÜR DIE PATHOLOGIE Prof Dr Arthur Biedl
4 ed Berlin & Vienna, 1922 Urban and Schwarzenberg
Band I, 1 Teil, 338 p, Band III, 480 p, 8°

The readers of this Journal will be very glad to know that a new edition of Biedl's well known monograph is now coming from the press. No endocrinologist needs a detailed introduction to a work which has so long been our standard authority.

Part 1 of Volume I includes a general introduction in which appears a particularly welcome fifty-page discussion of "constitutional" biology, a topic upon which there has been much loose writing. Several instructive diagrams are used to bring out the proportional bodily differences at various ages in both sexes. The factors determining "constitution" are carefully considered. The next fifty-six pages are given to methodology. The last two hundred pages are devoted to the thyroid and parathyroid glands.

Volume III is made up entirely of bibliography. Some citations as late as 1921 are found. It is gratifying to note that, as in previous editions, the original captions of the articles cited are included. Endocrinologists are much indebted to Prof. Biedl for the vast amount of irksome labor that the compilation of this volume has entailed.—R. G. H.

THYMUS UND BASEDOW, EIN BEITRAG ZUR FRAGE DER BEZIEHUNGEN
BEIDER ORGANE Dr. Erich Junge Berlin, 1921 Verlag von
Emil Ebering 18 p

The text of this brochure is as confused as its title. Some data are adduced as to whether the thymus should be removed in Graves' disease. A few pages are also devoted to "Thymus-tod." The author speaks of vagotonia as though the theories of Eppinger and Hess were established facts. More details are unnecessary.—J. K.

THE PITUITARY Prof. W. Blair Bell London, 1919 Balliere,
Tindall & Cox 347 p

This book is an excellent, well illustrated monograph on the physiology, anatomy, pathology and pharmacology of the hypo-

physis Every important question is thoroughly discussed with a good review of the literature and the author's own opinion is often given at the end

For the most part, the literature is reviewed only through 1913 or 1914 The clinical part of the book is not always satisfactory, diabetes insipidus, Frohlich's disease, etc., are simply described as being caused by a disease of the pituitary, while even in 1897, Loeb firmly denied this and considered that these are diseases of the midbrain It is not mentioned that at least 40 per cent of acromegalics are also afflicted with a strange form of diabetes mellitus The book has been read with much interest, and it is warmly recommended —J K

PRACTICAL CHEMICAL ANALYSIS OF BLOOD Victor C Myers St Louis, 1921 C V Mosby Co 121 p, 8°

In the endocrinopathies practical blood chemistry is becoming of increasing importance In Myers' book will be found a terse and readable presentation of the data needed in making determinations of blood constituents in studies of blood sugar curves, blood urea, etc It will be found especially useful in the more careful studies in diabetes —R G H

Abstract Department

A case of ACROMEGALY Faber (K), Ugesk f Læger (Copenhagen), 1919, 81, 1400-1403

A typical case of acromegaly Examination in August, 1911, showed a total hemianopsia and diminishing of the other part of the visual field Renewed examination in September, 1911, showed the visual field enlarged in both eyes and the left hemianopsia complete for red, but not for white In 1919 the left visual field was normal X-ray treatment was followed by considerable improvement

—K H K

A case of ACROMEGALY (Een geval von acromegalie) Tempelmans Plat, Maandbl v Specialische Geneesk (Amst), 1922, 5, 8

Demonstration of a case No details are described —J K.

Examination of a boy with ADIPOSITY Begtrup (E), Ugesk f Læger (Copenhagen), 1921, 88, 923-929

In a boy, aged 11 years, with very marked adiposity there was found normal total metabolism This was diminished by a stringent four months' limitation of diet At the same time the protein and fat of the food were better utilized It was very easy to obtain N-balance, even with low protein and low calorie diet No endocrine disturbances could be recognized —K H K

Clinical ADRENAL insufficiency (Études cliniques sur l'insuffisance surrénales) Babonneix (L), Monde Méd (Par), 1917, 26, 225-229

Reference verified from Index Medicus

The pathogenesis of Addison's disease Destruction of the ADRENAL medulla by a metastatic lymphangio-endothelioma of the peritoneum (Zur Pathogenese des Morbus Addisonii Zerstörung des Nebennierenmarkes und des Grenzstranges durch ein Lymphangio-endothelioma peritonei metastaticum) Bannwart (A), Frankfurt Ztschr f Path (Wiesb), 1921, 26, 307-316

The author refers to some cases of Addison's disease reported recently by Fahr and Reiche (Frankfurt Ztschr f Path, 1920, 22, 231-253), which supported the view that the suprarenal cortex was the primary seat of the disturbance causing Addison's disease He reports the case of a male white subject, aged 45 years, from Hedingger's Laboratory at Basel The patient was under observation approximately two years and died with a clinical diagnosis of Addison's

disease and malignant tumor of the peritoneum The autopsy showed lymphangio-endothelioma of the peritoneum with metastases into the skin, subcutaneous fatty tissue, bone marrow, cervical mediastinum, bronchial, retroperitoneal and mesenteric lymph glands, lungs, pleura, thyroid, spleen, liver, intestine, both suprarenals, and both testes The thymus was not made out The spleen was slightly enlarged The left adrenal was markedly enlarged with consistency increased, the cortex was approximately 3 mm in thickness and poor in lipoid Demarcation between the medulla and cortex was not made out The right suprarenal was slightly larger than left, measuring $6 \times 7 \times 1.5$ cm Microscopic examination showed that the medulla of both suprarenals had been completely destroyed by tumor metastases while the cortex was well preserved Bannwart thinks the case demonstrates with great clearness that typical Addison's disease may develop from isolated disease of the suprarenal medulla, thus supporting Wiesel and Heding in their contention that the malady is primarily a disease of the chromophil system —D M

(ADRENIN) Remarks on caffein glycosuria (Remarques sur la glycosurie caféinique) Bardier (E), Ducheln (P) & Stillmunkès (A), Compt rend Soc de biol (Paris), 1922, 86, 4-6

Of endocrine interest in that the antagonistic action of adrenalin and caffein on the peripheral termination of sympathetic nerves is discussed —T C B

The effects of ADRENAL feeding upon the iodine content of the THYROID gland Black (E M), Hupper (M) & Rogers (J), Am J Physiol (Balt), 1922, 59, 222-226

Dogs were fed on a standard diet to which was added either "adrenal residue," or adrenal nucleoprotein, or adrenalin crystals (P D & Co) The controls were fed the standard diet only One lobe of the thyroid was removed before beginning the experiment, and its iodine content determined by the Kendall method After forty-five days of feeding the second lobe was removed and its iodine content determined Adrenal residue can produce in the dog's thyroid a gain in iodine of an average of seventy per cent in forty-five days Adrenal nucleoprotein causes a gain in iodine of fifty per cent Adrenal crystals produce little if any gain The extract of the entire gland, containing something more than pure adrenalin, therefore, has a direct effect upon the thyroid —T C B

Calorigenic effect of ADRENALIN in dogs Boothby (W M) & Sandiford (I), Am J Physiol (Balt), 1922, 59, 463-464

Subcutaneous injection of 0.5 mgm adrenalin in man causes an increase in the rate of heat production The rate of absorption of adrenalin approximates 0.0016 mgm per kilo per minute When

injected at this rate in dogs there is just a perceptible calorogenic effect Intravenous injections of 0.0045 mgm per kilo per minute produces a definite calorogenic effect of from 10 to 40 per cent These figures are comparable with those obtained by Stewart and Rogoff and by Cannon under normal conditions, and lead to the conclusion that the adrenals can spontaneously discharge sufficient adrenalin to effect the rate of heat production, possibly by chemical stimulation of cellular activity—T C B

(ADRENAL) Pathogenesis of gastric ulcers (*Contributo sperimentale alla patogenesi dell'ulcera gastrica*) Brisotto (P), *Riforma med* (Napoli), 1922, 38, 127-129

Brisotto reports a case of a dog, which, after removal of an adrenal, showed asthenia, gastric disturbances with vomiting, and at autopsy a pyloric ulcer involving the muscularis and mucosa Similar results were obtained through operations on the vagus and on the celiac plexus, though the ulcer was not always found—G V

SUPRARENAL insufficiency and organotherapy Cohoe (B A), *Penn M J* (Harrisburg), 1922, 25, 345-346

A brief résumé of the acute, subacute and chronic types supposedly dependent upon suprarenal insufficiency, acute rapidly fatal cases are thought to be due to hemorrhage into the suprarenals, Addison's disease is referred to, the chronic functional type with asthenia, lethargy, circulatory weakness, cold hands and feet is mentioned The author is conservative in his statements concerning organotherapy with suprarenal extracts, seeming to agree with those who report little or no benefit from their use He distinguishes between the drug effect of epinephrin, as used prophylactically in anaphylactic shock or to abort attacks of asthma, and any supplementary rôle in so-called states of suprarenal insufficiency There is no certain evidence that suprarenal extract given by mouth has any curative power—H L

(ADRENAL) Therapeutic value of "adrenofer" (*Ricerca sul valore terapeutico dell'adrenofer*) Connio (A) & Crosa (A), *Gazz med sicil* (Catania), 1917, 19, 344-346

Reference verified from Index Medicus

Blood pressure and pulse reactions to ADRENIN in sick children (*Modificazioni della pressione e del polso per effetto dell'adrenalina in bambini ammalati*) De Angelis (F), *Pediatrics* (Napoli), 1921, 29, 542-547

The effect of adrenalin on sick children as regards the kind of reaction provoked by the individual pathological condition and the possibility of a special reaction in special groups or types of disease has been studied The author found that the injection of adrenalin

(1 cc, 1 1000) causes in sick children a rapid rise of the pressure, manifest after the first 10 minutes, reaching its maximum within 30 minutes, to slowly decrease in from 2½ to 3½ hours. Both maximum and minimum, but especially the maximum pressures were studied. Children with cardiac or cardio-vascular disorders showed a reaction less marked and of shorter duration than normal. The pulse showed initial acceleration, followed immediately by retardation, but maintaining strong systolic tension—G V

Complementing activity of the blood serum with relation to ADRENAL insufficiency Ecker (E E) & Rogoff (J M), J Immunol (Balt & Cambridge, Eng), 1921, 6, 355-361

The rabbit was used in these experiments because of the fact that a fair proportion of these animals survive complete bilateral adrenal ablation. Accessory adrenal tissue is sometimes present in the rabbit, it always consists of cortical substance and not medulla. At autopsy upon the six rabbits used only one was found to still possess a small mass of adrenal tissue near the liver. An antisheep hemolytic system was employed, the complement being supplied in quantities of 0.025 to 0.2 cc of the serum of the epinephrectomized rabbits. The authors conclude that the complementing power of the blood serum of rabbits is not modified by unilateral or bilateral adrenal extirpation—J P S

Raynaud's syndrome in ADRENAL disease Faber (K), Ugeskrift for Læger (Copenhagen), 1919, 81, 2112-2114

A woman, aged 47 years, showed typical symptoms of Raynaud's disease, cyanosis, coldness of the fingers, paronychia, and later on, gangrene of one finger. She suffered with edema of the legs and sometimes of the face. After a month, the patient became nauseated. There was further pigmentation of the skin, albuminuria and, lastly, convulsions and death. Autopsy showed the left adrenal gland normal, the right adrenal gland was destroyed by tuberculosis, the kidneys showed nephritic changes. The thyroid, hypophysis and thymus were normal—K H K

The pigments of the ADRENALS Findlay (G M), J Path & Bacteriol (Cambridge), 1919, 23, 482-489

There is a striking similarity between the distribution of the vegetable lipochromes and one of the accessory food factors, fat soluble A. The author studied the content of fowl and human adrenals in lipochrome and melanin. The amount of lipochrome in the adrenals of hens can be varied by alterations in the lipochrome content of the food. He found, in addition to carotin and xanthophyll, a possible third substance in the hen's adrenals that seems to be related to the lipochromes. In acute pathological conditions in human beings, e. g., in acute infections such as pneumonia and

meningitis, the amount of lipochrome pigment in the adrenals is moderately increased. No melanin pigment was found. In chronic affections, such as carcinoma, tuberculosis and diabetes, the lipochromes showed a considerable increase and there was almost always some melanin present both in the cortical and in the medullary cells. Since lipochrome pigment is of exogenous origin, its presence in the adrenals must be looked upon as a true infiltration, analogous to fatty infiltration and occurring in conditions involving a decrease in the activity of the cell. Melanin pigment, on the other hand, appears to be entirely endogenous in its origin, and to be formed in conditions of long-continued depression of the cell. Such depression may arise physiologically in infancy and old age, and in almost all chronic pathological conditions, more particularly in tuberculosis and cancer.—J P S

The diaphoretic action of ADRENIN (Ueber die bei iontophoretischer Einführung von Substanzen zu beobachtenden Hautreaktion) Freund (E), Ztschr f phys u diätet Therap (Leipz), 1921, 25, 145-160

Adrenalin acts as a stimulant to the local secretion of sweat in man. In the reaction the local application of heat plays a significant rôle. The antagonistic action of adrenalin and pilocarpin can be seen in the vasomotor apparatus of the skin.—F S H

(ADRENIN) The secretion of sweat, Part 1 Supposed inhibitory nerve fibers on the posterior nerve roots. Secretion after denervation. Langley (J N), J Physiol (Lond), 1922, 56, 110-119

Of endocrine interest in that it is shown that adrenalin only causes secretion of sweat by virtue of the fluid in which it is dissolved, Ringer's solution injected into the pad of a cat's foot commonly causing more secretion of sweat than does adrenalin.—T C B

ADRENAL function III Variations in the vasomotor action of the great splanchnic nerve in various species of animals. Gley (E) & Quinquaud (A), J de physiol et de path gén (Par), 1921, 17, 355-364

Observations on dogs, cats, rabbits, and a fox show that the form of reaction following splanchnic excitation differs in different species of animals. This fact does not lend support to the theory that the reaction depends in part on the adrenal secretion.

—Chem Abst, 16, 754

Pathological ADRENAL alterations in domestic animals (Le alterazione delle capsule surrenali in rapporti di diversi stati patologici degli animali domestici) Grimaldi (E), Clin vet (Milano), 1917, 39, 671-700

Reference verified from Index Medicus

Epilepsy and hyperfunction of the ADRENALS (*Krampfkrankheiten als Hyperfunktion der Nebenniere*) Hanke, Deutsche med Wchnschr (Berl), 1922, 48, 119

The author removed an adrenal in two cases of epilepsy In one case there was a slight temporary result, in the other, no result whatever was seen —J K

The relation of the ADRENALS to fatigue Hartman (F A), Am J Physiol (Balt), 1922, 59, 463

The denervated pupil (superior cervical ganglion removed) of a normal cat usually dilates after working in a treadmill for a time Dilatation increases as the work proceeds Removal of both adrenals abolishes the "fatigue" dilatation Cutting the splanchnic to a single remaining adrenal reduces or abolishes "fatigue" dilatation Cats with but a single adrenal, and that denervated, cannot work so hard, nor travel so far, as normal animals After regeneration of the nerve, the pupil reaction reappears, and the animal works better Epinephrin increases the ability to do work and withstand fatigue —T C B

Action on blood pressure of ADRENIN injected into the subarachnoid space Kasahara (M), Kyoto Igakkwai Zashi, 18, No 2, Abst , Jap Med World (Tokyo), 1921, 1, 26

Injection of commercial adrenalin into the subarachnoid space of the rabbit causes a lowering of blood pressure due to the acidity of the preparation The work of Meltzer and Auer along this line has no clinical significance An injection of 0.7% saline into the subarachnoid space without first removing cerebrospinal fluid causes a rise in pressure in both the cerebrospinal cavity and the blood vessels This rise is slow and is maintained for a comparatively long period Clinically subarachnoid injection of adrenalin has no more influence than 0.7% saline —R G B

ADRENAL toxic serum and atheroma Marabotto (F), Ann d Ist Maragliano p la cura d tuberc , etc (Genova), 1918, 8, 209-224

Reference verified from Index Medicus

The influence of ADRENIN anemia on the progress of experimental tuberculous infection (*L'influenza dell'anemia adrenalinica sul decorso della infezione tubercolare sperimentale*) Maragliano (D), Riforma med (Napoli), 1921, 37, 1082

Adrenalin anemia renders more severe local alterations due to inoculation of tuberculous products The invasion into the neighboring ganglia and the generalization of the process are not influenced —G V

Influence of glands with internal secretions on the respiratory exchange III Effect of SUPRARENAL insufficiency (by removal) in thyroidectomized rabbits Marine (D) & Baumann (E J), Am J Physiol (Balt), 1922, 59, 353-368

In a previous paper it was shown that removing or crippling the suprarenals resulted in marked changes in the respiratory exchange, and possible causes of increased heat production were discussed. The present paper describes experiments undertaken to obtain data on the question whether the thyroid is an important factor in the increased heat production following suprarenal ablation. The procedure was to observe the normal heat production in six rabbits for two weeks, then completely remove the thyroids and measure heat production, then remove the suprarenals and again observe the heat production until the animals died or were sacrificed. Protocols in full are given, with a discussion of the results. The conclusion is that removal of the thyroid prevents or greatly lessens the increased heat production caused by partial destruction of the suprarenal cortex. While epinephrin in large doses may stimulate the thyroid, the insufficiency of the regulatory, inhibitory and restraining effects of the cortical influence is much more important in thyroid activity and tissue oxidations in rabbits. Glandular interrelations such as the gonads may be involved (See also Am J Physiol, 1922, 59, 439-440) —T C B

The influence of ADRENALIN on metabolism in isolated skeletal muscle Martin (E G) & Armitstead (R B), Am J Physiol (Balt), 1922, 59, 37-43

Boothby and Sandiford report a "specific dynamic action of adrenalin chloride on all the cells of the body causing them to metabolize more rapidly under its influence." Metabolism proceeds in isolated muscle with the production of heat and carbon dioxide, and it is this metabolism that is investigated. The method proposed by Haas was modified to suit the special requirements. The sartorius muscles of the frog were carefully excised, weighed, and suspended in neutral Ringer's solution to which had been added eight drops of 0.02 per cent phenolsulphonephthalein solution. All gaseous exchange with the outside air was guarded against. When the color of the solution had definitely changed (about 20 minutes) the muscles were removed, the pH of the solution again determined, and the production of H ions per gram of muscle computed. By this means it was determined that the excised sartorius during the first half hour after excision averages a pH production of 110×10^{-8} at 20 degrees C. The addition of adrenalin to the solution augments this resting metabolism from 25 to 400 per cent, according to the concentration of the adrenalin. This is interpreted as confirming the view of Boothby and Sandiford —T C B

(ADRENAL) Addison's disease (Morbo di Addison) Molinari (G),
Riforma med (Napoli), 1921, 37, 1024-1026

The article is a thorough discussion of Addison's disease as regards the most recent conceptions of its etiology and nature. The author insists on a primary adrenal as well as sympathetic etiology. He values highly whole adrenal gland treatment and favors the use of adrenalin only in emergency cases—G V

ADRENAL hematomas (Contributo allo studio degli ematomi delle capsule surrenali) Moramarco (G), Riv osp (Roma), 1916, 6, 1-17

Reference verified from Index Medicus

The influence of ADRENIN on blood sugar (Über die Wirkung des Adrenalins auf den Blutzucker) Petenyi (G) & Lax (H),
Biochem Ztschr (Berl), 1921, 125, 272-282

These observations were made in the First Medical Clinic of the University of Budapest. The authors determined the influence of subcutaneous injections of epinephrin in four adults, two children about the age of puberty, and four nursing infants. The dosages used were 10 mg, 0.6 mg and 0.1 to 0.3 mg epinephrin, respectively, for the three age groups. The blood sugar was determined by the Bang procedure one, two, three, four, six and eight hours after the injections. Invariably they observed hyperglycemia followed by hypoglycemia as has been reported by many others. In addition to the above mentioned normal subjects, they studied the effect of epinephrin injection in sixteen nursing infants suffering from infantile tetany. In these cases hyperglycemia following epinephrin injection was less marked than in normal individuals and did not always occur, while hypoglycemia always followed, just as in normal persons, and was even more pronounced in degree and duration—(D M) E J B

(ADRENIN) Urine formation in the perfused kidney. The influence of alterations in renal blood pressure on the amount and composition of urine. Richards (A N) & Plant (O H), Am J Physiol (Balt), 1922, 59, 144-183

It was found that increased urine flow follows administration of adrenalin as well as splanchnic stimulation—T C B

Urine formation in the perfused kidney. The influence of ADRENALIN on the volume of the perfused kidney. Richards (A N) & Plant (O H), Am J Physiol (Balt), 1922, 59, 184-190

"When the kidney of the dog or rabbit was excised and perfused with hirudinized blood at a constant rate of flow, the addition

of a small amount of adrenalin to the blood caused rise in perfusion pressure and swelling of the kidney This result is interpreted as evidence that the vas efferens is constricted by adrenalin with consequent rise of intraglomerular pressure and distention of the Malpighian bodies It is regarded as explanatory of the diuresis caused by adrenalin, splanchnic stimulation and medullary stimulation"

—T C B

The action of minute doses of ADRENALIN and PITUITRIN on the kidney Richards (A N) & Plant (O H), *Am J Physiol* (Balt), 1922, 59, 191-202

If adrenalin causes a rise of perfusion pressure, increased volume of the kidney and diuresis in the perfused kidney, it is believed that similar conditions might be demonstrated in the intact animal The essential difference would be that in the perfused kidney the blood is driven at a constant rate through the kidney regardless of the state of constriction of the blood vessels, while in the intact animal the renal blood flow would be diminished by vasoconstriction In attempting to solve this problem rabbits, cats and dogs were used The rabbits were made diuretic before the operation by feeding carrots, the dogs by injecting glucose solution into the stomach some hours before the experiment Carotid pressure was recorded Injections were into the jugular vein, and were not "washed in" Some animals were completely eviscerated after ligating all the coeliac and mesenteric arteries and the portal vein, in other the coeliac axis was not ligated, and only the jejunum, ileum and large intestines removed The vagi and splanchnic were cut Both suprarenal veins were ligated and the right kidney was ligated in some, excised in others After ligature of the abdominal aorta below the origin of the left renal artery, the inferior vena cava was prepared for the Barcroft-Brodie method of estimating blood flow through the kidney The volume of the left kidney was recorded by an oncometer and the urine flow by the drop method from a cannula in the left ureter "Under the influence of minute doses of adrenalin and pituitrin, blood flow through the kidney may be decreased, while the kidney volume and urine elimination may be increased Considerations are presented in support of the belief that this combination of events reveals a slight degree of constriction of the efferent vessels, with consequent increase in glomerular pressure The experiments are interpreted as bearing upon the problem of glomerular regulation of urine formation"—T C B

On the ADRENALIN content of the suprarenal capsules, determined by chemical methods and by physiological methods (*Sur la teneur en adrénaline des capsules surrénales, déterminée par la méthode chimique et par la méthode physiologique*) Richaud (A), *Compt rend Soc de biol* (Par), 1922, 86, 26-28

A comparison of the effects of pure l-adrenalin with solutions of the dried and powdered suprarenals of commerce, using the blood pressure curve as an index of their potency, after the method of Cushny. The curve furnished by 0.00002 gm adrenalin is duplicated by 0.0025 gm dried capsule, which corresponds to 0.0000066 gm of adrenalin calculated from the chemical titer. Either there are other pressor substance in the capsule, or the process of extraction does not furnish the total quantity of adrenalin present. The latter is most probable.—T C B

Cheyne-Stokes respiration, Part 1. Production by ADRENALIN
Roberts (F), *J Physiol (Lond)*, 1922, 56, 101-109

In a previous paper (*J Physiol*, 1921, 55, 346) the author mentions that rabbits and cats exhibit Cheyne-Stokes respiration after the intravenous injection of a large dose of adrenalin. The present paper describes the character of the respiration, and explains the cause. If a certain blood pressure is necessary to provoke respiration it may be that Cheyne-Stokes respiration has a vascular origin. To test this, rabbits were used. The blood pressure can be taken in the circle of Willis simultaneously with the carotid pressure by introducing a cannula into the common carotid close to the bifurcation into internal and external, the latter being tied off. The pressure in the circle of Willis rises and falls with that in the carotid, and is surprisingly high, being very little less than in the aorta. It may reach 160 mm or more after the injection of adrenalin. The number of experiments is not given, but the tracings show that as the pressure reaches the maximum after the injection of adrenalin apnea comes on, to give place to a resumption of respiration as the pressure falls. This is continued rhythmically. The conclusion is that the Cheyne-Stokes respiration sometimes produced by the injection of adrenalin is of two kinds: major waves with a periodicity of 30 to 80 seconds, and minor waves with a periodicity of 5 to 15 seconds. The first are due to rhythmic changes in the caliber of the cerebral vessels, the second seem to be associated with oscillations in general blood pressure.—T C B

Experimental study of clinical application of ADRENALIN Sorna (D), *Gun-i-dan Zasshi*, No 105, *Abst, Jap Med World (Tokyo)*, 1921, 1, 23

The adrenalin used was that of Sankyo and Co., Tokyo. It was assayed by the Meltzer-Ehrmann frog-eye method. For clinical administration adrenalin should be diluted with distilled water, 0.1% hydrochloric acid or 2.0% boric acid, and is best given by intravenous injection. When given hypodermically in a large quantity of physiological saline or sodium bicarbonate (1% solution) or through a steam inhaler its efficacy is greatly diminished.—R G B

ADRENAL extirpation in epilepsy (Nebennierenevstipation bei Epilepsie) Sultan (G), Deutsche med Wchnschr (Berlin), 1922, 48, 153-155

In 5 cases of epilepsy an adrenal was removed In 2 cases the blood pressure was somewhat raised after the operation, in a third, it was slightly lowered Schlund has stated that after the operation lymphopenia with neutrophilic leucocytosis is found This is true, but it is seen also after simple ether narcosis In one case the blood sugar was somewhat increased, in the four other cases the operation had no effect whatever The effect of the operation on the epilepsy was almost absolutely negative—J K

The action of **ADRENIN** on the surviving uterus (Umkehr der Adrenalin-wirkung auf den überlebenden Uterus durch Ionenverschiebung) Turolt (M), Arch f gynaek (Berl), 1922, 115, 600-610

An excess of potassium or calcium salts in the nutrient solution in which the surviving uterus from either guinea-pig or man is suspended causes a change in stimulation of this tissue While adrenalin inhibits the movements of the gravid and non-gravid uterus of the guinea-pig in normal Ringer's solution, when an excess of calcium is present, stimulation by adrenalin takes place in both cases On the other hand, potassium salts which inhibit the rhythmic movements have no effect on the adrenalin action On the human uterus, however, which adrenalin stimulates in either the gravid or non-gravid condition, an excess of calcium produces inhibition of automaticity, and potassium an augmentation The inhibitory action of the calcium only hinders the adrenalin action on the non-gravid These studies show that the two ions, calcium and potassium, have exactly the opposite effect from adrenalin on both uterus preparations—F S H

(**ADRENAL**) Addison's syndrome in incomplete Recklinghausen's disease (Sindrome addisoniana in una forma incompleta di malattia Recklinghausen) Vignolo-Lutati, Riforma med (Napoli), 1917, 32, 1061-1064

Reference verified from Index Medicus

Sudden death in atrophy of the **ADRENAL** cortex (Ueber plotzliche Todesfälle bei Atrophie des Nebennieren-markes) Zimmerman (R), Monatschr f Geburtsh u Gynaek (Berl), 1922, 56, 259-270

Report of two cases as described in title No marked pigmentation was present—F S H

Criteria in "**CONSTITUTION**" researches (Über Konstitutionsforschung in der normalen Anatomie Einige Richtlinien) Hammar (J A), Anat Anz (Jena), 1916, 49, 449-474

DIABETES Barlaro (P M), Prensa méd argentina (Buenos Aires), 1916, ii, Suppl., 218-220

Reference verified from Index Medicus

DIABETE ed acidosi Castellino (P), Folia med (Napoli), 1917, 745, 694-817

Reference verified from Index Medicus

A method to determine acetone, diacetic acid, oxybutyric acid and dextrose quantitatively in DIABETIC urine Claudius (M), Hosp-Tid (Copenhagen), 1921, 64, 97-108

The author describes in detail a method to determine quantitatively the substances named. The principle is oxydizing with sodium iodide and sulfuric acid. The precipitated iodide is absorbed by tetrachlormethane and titrated with thiosulfate—K H K

Treatment of DIABETES in common practice Hagedorn (H C), Ugesk f Læger (Copenhagen), 1919, 81, 1939-1945

The author describes the theoretical foundation for the American treatment of diabetes (Allen and Joslin). He further describes the manner in which the practitioner can best carry out this treatment—K. H K

The duration of fatal attacks of DIABETES mellitus Heiberg (K A), Hosp-Tid (Copenhagen), 1919, 62, 1137-1140

Examinations of reports of fatal diabetes during a period of 10 years in Danish towns (820 men and 683 women) shows that the duration of the disease is much longer in old age than in youth and much longer for men than for women. However, the apparent longer duration in men may be due to the fact that men have their urine examined for life insurance oftener than do women—K H K

(DIABETES) Case of glycosuria of combined nature Holst (J E), Ugesk f Læger (Copenhagen), 1921, 83, 1072-1081

The author reports the case of a man, aged 47 years, with glucosuria, which shows a transition form between true diabetes and the so-called renal diabetes. The result of the blood-sugar examinations (fasting and eating sugar on bread) is illustrated by a curve. The case shows continued glucosuria with very low blood-sugar, absence of diabetic symptoms, no progression for 23 years (without treatment), but blood-sugar curves corresponding to those which are found in true diabetes—K H K

The problems of modern DIABETIC treatment Janney (N W), Northwest Med (Seattle), 1922, 21, 47-49

An analysis of the most recent 100 cases of diabetes observed by Janney, shows that 87 per cent had received previous medical treatment. Of this number 79 per cent had merely received qualitative restrictions of diet, but only 21 per cent accurately weighed diets. The author, with this experience as a text, criticizes the methods of the average general practitioner and even general internist, and insists that very few of them are equipped to manage this disease properly, with the result that the mortality is considerably higher than it should be. Some blame also attaches to the patient who refuses to follow directions, even though attractive menus are offered him. "In all but the very lightest cases a strict quantitative diet must be enforced over a long period, in all severe cases, for the duration of the patient's life." The exacting necessities of modern diabetic treatment demand a diabetic laboratory, an adequate clinical chemical laboratory, professional judgment, skill and experience. All new hospitals should include a metabolic pavilion with commodious diet kitchen, chemical and respiratory metabolic laboratory, sick rooms, a diabetic class and an out-patient department with instruction of the poor in diabetic cookery—H L

The use of raw starch in the treatment of DIABETES Knerr (E B), J Missouri M Ass (St Louis), 1916, 13, 442-445

Reference verified from Index Medicus

Negligible GLYCOSURIA Leyton (O), Practitioner (Lond), 1922, 108, 113-118

The author introduces the term "negligible glycosuria" in preference to "diabetes innocens" "renal glycosuria" and "glycosuria without hyperglycemia." He refers to that group of people who excrete about 0.5 per cent dextrose in their urine, but have no other manifestation of diabetes mellitus. He prefers the term "negligible glycosuria" because the cause of the condition is not known. These cases are not early diabetes mellitus. Neither the quality nor quantity of food consumed makes any appreciable difference to the percentage of sugar in the urine excreted. These cases should not be confused with true diabetes mellitus. They do not require any treatment. Leyton has examined 18 such individuals in the past two years. He noted a familial tendency. Seven cases are mentioned that have histories of glycosuria averaging 18 years and none has developed symptoms or signs of diabetes mellitus—H L

Influence of lumbar puncture on the polyuria and glycosuria of DIABETES mellitus (Influence frénatrice de la ponction lombaire sur la polyurie et la glycosurie du diabète sucré) Lhermitte (J) & Fumet (C), Bull et mém Soc méd d hôp de Par, 1922, 46, 322-328

Lumbar puncture in 2 cases of diabetes mellitus brought about a diminution in urinary secretion and sugar elimination This may indicate a central origin for the disease—F S H

Emotional DIABETES in forensic medicine (*Il diabete mellito da emozione in medicina legale*) Maganami (R), Arch di antrop crim [etc] (Torino), 1916, 37, 181-194

Reference verified from Index Medicus

Sparing action exercised by the fats against the destruction of protein in DIABETICS in a state of nitrogen denutrition (*Action d'épargne exercée par les graisses vis-à-vis de la destruction d'albumine chez les diabétiques en état de dénutrition azotée*) Maignon (F), Compt rend Soc de biol (Par), 1922, 86, 111-114

Deals with the sparing action of fats and a treatment of diabetes based upon it—T C B

Mastoid operation in DIABETES Mygind (H), Hosp-Tid (Copenhagen), 1921, 64, Oto-laryngeal Soc Reports, 108-111

Since 1905 the author has treated 1500 patients with acute suppuration of the middle ear Only 6 of these were complicated with diabetes, 5 of them were operated upon Four died in coma within a few days after the operation The complication of diabetes with otitis media is rather rare, but the prognosis is bad Perhaps the coma is produced by a shock effect—K H K

DIABETES in the son of a syphilitic (*Diabète avec aréflexie chez un fils de syphilitique*) Pinard (M) & Mendelsohn (E), Bull et mem Soc med d hôp de Par, 1922, 46, 397-404

Antiluetic treatment of this case resulted in disappearance of sugar from the urine—F S H

Hypophysis extract in DIABETES mellitus (*Sulla efficacia degli estratti ipofisari nella cura del diabete mellito*) Vigevani (G), Osp maggiore (Milano), 1917, 4, 530-533

Reference verified from Index Medicus

The therapeutic action of pituitrin in DIABETES INSIPIDUS (*Sur l'action thérapeutique de la pituitrine dans le diabète insipide*) Démètre (P E), Bull et mém Soc méd d hôp de Par, 1922, 46, 308-314

In diabetes insipidus a renal element is present which is associated with a permanent deficiency of pituitary secretion This secretion has a direct action on renal as on all other epithelium The influence of the hypophyseal secretion is sufficient to explain the mechanism of the polyuria in diabetes insipidus Pituitrin exerts a direct and transitory effect on the polyuria.—F S H

Infundibular polyuria. Syphilitic **DIABETES INSIPIDUS** (*La polyurie infundibulaire La diabète insipide syphilitique*) Lhermitte (J), *Ann de méd (Par)*, 1922, 11, 89-127

A review and discussion of the origin of diabetes insipidus together with the presentation of certain histological studies of infundibular-tubercular lesions of syphilitic nature. These studies showed that the lesions were limited exactly to the infundibulum and the tuber cinereum. The lesions were meningeal, vascular and neural. That the processes were syphilitic inflammations was undoubted. These facts contribute considerable doubt as to the soundness of the idea that the polyuria of diabetes insipidus takes its origin directly, if at all, in the hypophysis.—F S H

(**ENDOCRINE ORGANS**) Further studies on substances with specific action prepared from single organs. VI (*Weitere Untersuchungen über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung*) VI) Adberhalden (E) & Gellhorn (E), *Arch f d ges Physiol (Berlin)*, 1922, 193, 47-83

(See *Endocrinology*, 5, 643) The testis optones obtained by hydrolysis with 10 per cent sulphuric acid excite the automaticity of quiescent frog heart-strips, while the hydrolysate produced by enzyme and autolytic action has no such effect. Subsequent hydrolysis of the latter with 10 per cent sulphuric acid gives a product with the characteristic action. This is strengthened by removal of substances soluble in alcohol. Enzyme-produced placenta optones increase the contractions of Straub's preparations after pulse diminution, while acid-produced optones from placenta produce only a negative inotropic action (and a negative chronotropic action on heart-strips). Thyroid and struma hydrolysates excite the automaticity and tonus of surviving frog esophagus. In the same concentration placenta optones (acid or enzyme produced) are markedly paralyzing, the acid optone in weaker concentration increases the contractions. Thyroid, pituitary, thymus, ovary, placenta (enzyme) and testis (acid) optones exercise a more or less strong capillary dilating and sometimes artery dilating effect, and inhibit or lessen the action of adrenalin. It is suggested that these "incretions" play a significant rôle as regulators of the capillary mechanism.—A T C

Uricolytic power of the ENDOCRINE glands (*Sul potere uricolitico delle ghiandole e secrezione interna*) d'Amato (L) & de Nunno (R), *Pathologica (Genova)*, 1917, 9, 205-210

Reference verified from *Index Medicus*

PLURIGLANDULAR insufficiency Askgaard (V), *Hosp-Tid (Copenhagen)*, 1921, 64, *Neurol Soc Reports*, 19-20

A girl, aged 10 years, since her fifth year had complained of headache and dullness. She had always been very fat. The

following symptoms were manifested convergent strabismus, adiposity, and shortness of arms and fingers X-ray examination showed irregularity of the epiphyseal lines as in achondroplasia
—K H K.

(INTERNAL SECRETION) Multiple calcification of the muscolo-tendinous sheets (*Sopra un caso di calcificazione multipla delle guaine muscolo-tendinee*) Cantelmo, Riforma med (Napoli), 1921, 37, 1083

The disorder in a subject, 25 years old, began with tumefactions, which, in a few months, opened, discharging a kind of calcareous paste formed of calcium carbonate and phosphate Both legs were affected, the process began with the vessels, their walls being thickened and lumen reduced There was also found atrophy of the muscles, protruding thyroid, sexual frigidity and asthenia The case is thought to be due to endocrine dysfunction—G V

ENDOCRINE deformity (Dismorfe endocrine) Giannuli (F), Riv di antrop (Roma), 1919, 21, 215-234

Reference verified from Index Medicus

Experimental studies on INTERNAL SECRETION Harada (S), Tokio Igakkwai Zasshi, Jap Med World (Tokyo), 1921, 1, 17-18

The author fed desiccated glands of internal secretion of cattle to tadpoles and young fish Controls were fed with liver Tadpole growth and metamorphosis was as follows Normally the right fore leg first began to develop, then both legs developed simultaneously, while the left leg developed first least frequently When fed with thyroid extract the frontal walls of the respiratory tube and margins of the tail fin disappeared first, then the left fore limb usually developed This might have been due to an abnormally augmented metabolism caused by the thyroid hormone These animals were found to have smaller thyroid and a smaller pituitary body, while the testes were larger than in the controls The range of stimulation by galvanotropism was greatly lowered, possibly due to hormonal control This change took place within a few hours and returned to normal in 3-4 days Iodothyryn as well as iodonal had nearly the same effect as thyroid Lipiodin and iodostarin produced no abnormal metamorphosis In thymus fed tadpoles metamorphosis was slightly retarded If the thymus was mixed with wheat flour there was an irregular course of development Thymus feeding had no marked effect on the range of galvanotropism Pituitary feeding caused an increase in the length of the body The relative increase in length was more marked when the posterior lobe alone was used Those fed with anterior lobe had a slightly large ovary, but a small pituitary and a small thyroid Adrenal cortex feeding caused poor growth The pancreas and the thyroid seemed

somewhat smaller Those fed with ovary had larger ovaries than the controls The effect on body growth was not mentioned The metamorphosis of the goldfish, *Oryzias latipes* and the carp have been similarly affected —R G B

Osteopsathyrosis and ENDOCRINE glands (*Osteopsatirosi e ghiandole endocrine*) Giorgi (E), *Riforma med* (Napoli), 1921, 37, 787

The post-mortem examination of a ten months' infant revealed a definite condition of fragilitas osseum with multiple fractures, there was found besides chronic hypophysitis, diffuse, irregular adrenal medulla and hyperplasia of the interstitial cells of the testis There had been in life a 3 plus cutaneous tuberculin reaction The initial cause is given as tuberculosis from a maternal focus, the determining endocrine dysfunction being a consequence of the infection

—G V

INTERNAL SECRETION and autolysis (*Autolisi e secrezioni interne*) Izar (G) & Fagnoli (A), *Sperimentale Arch di biol* (Firenze), 1916, 70, 265-327

Reference verified from Index Medicus

Action of the INTERNAL SECRETIONS upon experimental cancer Korentschewski & Kenow, *Soc Belga Biol*, 1920, (May), abst, *Pathologica* (Genova), 1922, 13, 60

Castration in the dog facilitates the development of sarcoma, but it does not have any influence on the cancer of mice Thyroidectomy seems to increase its development in dogs as well as in mice Thyroid feeding retards the development, thymus feeding increases it Mice fed with boiled tumor extract are less receptive than the controls —G V

(ENDOCRINE GLANDS) Treatment of the métrorrhagias of young girls (*Le traitement des métrorragies des jeunes filles*) Hartmann (H), *Gynéc et obst* (Paris), 1922, 5, 81-83

In a large majority of the transitory or prolonged changes in the menstrual flow there is an endocrine factor which has followed on from some infectious or chronic disease Daily administration of 25 mg thyroid extract, 0.20 gm pituitary extract and 0.05 gm adrenal extract is recommended —F S H

(ENDOCRINE GLANDS) Glandular dystrophies and particularly mono-symptomatic dystrophies (*Dystrophies glandulaires et particulièrement dystrophies mono-symptomatiques*) Hutinel (V) & Maliet (M), *Ann de méd* (Par), 1921, 10, 422-445

A continuation of the review previously noted —F S H

INTERNAL SECRETION and the hormones Krabbe (K H),
 Naturens Verden (Copenhagen), 1921, 1-8

A short popular review of the functions of the different glands of internal secretion —K H K

Modifications in the ENDOCRINE glands and blood of chickens injected with adrenalin and cholin (Modificazioni nelle ghiandole endocrine e nel sangue di polli iniettati con adrenalina e colina)
 Pighini (G), Bioch e Terap Sperim (Milano), 1921, 8, 140-154

Experiments with adrenalin (1% in dose of 1 cc) were made on 15 chickens ranging in age from 2½ to 18 months. The older subjects stood the injections much better than the younger. Cholin injections (1% cholin hydrochlorate, Merck) of 0.5 to 1 cc were made in 5 chickens from 2½ to 18 months of age. The organs examined besides the blood were the cerebrum, hypophysis, thyroid, liver, spleen, pancreas, kidneys, testes, ovaries, thymus and adrenals. The thymus, adrenals, spleen and blood showed much more accentuated histological changes than the others. The thyroid showed modifications with cholin injections. The other organs reacted only in case of acute intoxication, as in any toxic condition. In hyper-adrenalized animals there was found parenchymatous degeneration of the thymus, shown by extreme diminution of the lymphatic elements of the cortex, the reduction of Hassall's corpuscles, and lipoid degeneration of the epithelial elements. The Malpighian lymphoids of the spleen were greatly reduced, there was hypertrophy of the chromaffin tissue of the adrenals, with diminution of the lipoids of the cortex. There was neutrophil leukocytosis (pseudoeosinophilia) in the blood. Animals treated with cholin showed hyperfunction of the thymus with hypertrophy of the medulla, conspicuous increase of the Hassall's corpuscles, many forms of hypertrophy of the epithelioid cells (giant, myoid cells), colloidal cysts, and thyroid with Basedowian characteristics. In the spleen was hypertrophy of the Malpighian corpuscles. A tendency to hypertrophy of the cortex was found in the adrenals. There was slight polynucleocytosis. The relation of the foregoing data to the theory of adrenalin-cholin antagonism is discussed —G V

Subcutaneous calcifications in a case of PLURIGLANDULAR insufficiency Pontoppidan (B), Hosp -Tid (Copenhagen), 1921, 64, Dermatol Soc Reports, 12-13

A woman, aged 35, showed signs of myxedema and sclerodermia. During the last half-year there appeared under the skin in different places small tumours, which perforated and which contained masses of calcium phosphate, corresponding to the "granulomes calcaires sous-cutanées" of Millan —K H K

PLURIGLANDULAR syndrome with visceral inversion (Sindrome pluriglandolare in soggetto con inversione splanchnica total)
Rossi (A), Radiol med (Torino), 1916, 3, 20-23

Reference verified from Index Medicus

(**ENDOCRINOLOGY**) The influence of the parasympathetic nerve toxins upon blood sugar and adrenalin hyperglycemia Saito (I), Keio Igaku, 1, No 10, abst, Jap Med World (Tokyo), 1922 2, 50

In experimental studies it was found that stimulation of the peripheral ends of the parasympathetic nerves resulted in a decrease of the sugar content of the blood Hyperglycemia following administration of pilocarpin is not the result of the nerve stimulation, but of central asphyxia The parasympathetic nerves have no important relation to blood sugar since atropin sufficient to paralyze the peripheral structures causes no change The hyperglycemia following a large quantity of atropin is due to stimulation of the nerve centers The sympathetic and the parasympathetic nerves are antagonistic in their influence on carbohydrate mobilization Adrenalin hyperglycemia may be depressed by pilocarpin or eserine

—R G B-R G H

Biological remarks on constitution, ENDOCRINE ORGANS, internal metabolism and ions (Enkele biologische opmerkingen over constitutie, inwendige secreten, inwendige voeding, isolonie) de Somer, Geneesk Jaarboek v Vlaanderen (Gent), 1922, 2, 195-201

A short general review in which the author concludes that practically nothing is known of "constitution" or of endocrinology and that our knowledge on these subjects could be increased by a special study of colloids, electrolytes, and ions and their physico-chemical properties —J K

On the specificity of GASTRIN and pancreatic SECRETIN Luckhardt (A B), Henn (S C) & Palmer (W L), Am J Physiol (Balt), 1922, 59, 457-458

The presence of gastrin in the duodenal mucosa, liver and thyroids raises a doubt as to the physiological significance of this substance previously described as present in the gastric mucosa Gastrin is prepared from the duodenal mucosa in much the same way as is pancreatic secretin, and it seemed desirable to determine whether gastrin stimulates not only the stomach but also the pancreas, and whether pancreatic secretin could be prepared from gastric mucosa as well as intestinal, and stimulate both pancreas and stomach to secretory activity In dogs, the stomachs of which, provided with gastrotomies, were ligated at the cardia and pylorus,

and which, in addition, possessed pancreatic fistulae and jejunostomies, the deep muscular injection of gastrin prepared from gastric intestinal mucosa induced a pronounced secretion of gastric juice and a marked secretion of pancreatic juice. In such animals pancreatic secretin preparations, however made, stimulated not only the pancreas but greatly increased the volume and acidities of the gastric juice. There is no specificity of the so-called gastrins and secretins—T C B

A case of unilateral GIGANTISM Monrad (S), Ugeskr f Læger (Copenhagen), 1921, 83, 1375-1376

The author previously (1911, 1914) demonstrated 5 cases of unilateral gigantism and has later seen 3 other cases, one of which is described. In a girl, aged 11 months, the parents noticed difference between the extremities from the age of 3 months. The patient now shows very marked gigantism of the right side, especially of the forearm, nates and hip, and of the right side of the face and right labium majus. The tongue is symmetrical. X-ray plates show hypertrophy of muscles and subcutaneous tissue, but not of the bones. The ossification centres and epiphyseal lines are normal and symmetrical. There is no disturbance of the sella turcica. Pupils, hair, sweat, temperature, sensibility, reflexes and galvanic reactions are normal and symmetrical. The blood sugar is normal. There are no rickets, but slight symptoms of lymphatic diathesis, and slight eosinophilia. Of the 8 cases he has observed (3 boys and 5 girls) 4 were right sided and 4 left sided. Only in one case were the bones hypertrophied. In 6 cases the disease was congenital. In one case the gigantism was noted at the age of 2 years in connection with a nephrectomy for adrenal sarcoma—K H K

New views on the etiology of GLAUCOMA (Nuove vedute sulla etiologia del glaucoma) Paltracca, Riforma med (Napoli), 1921, 37, 763

The author believes that glaucoma is due in old people to an imbalance brought about by depressed production of hypotensive hormones, especially those of the testis and the ovary. The result of his observations follow. In young subjects (25-40 years) glandular therapy, either per os or by instillation, resulted in no modification in the intraocular tension, but always proved successful after the climacteric. In subjects with unilateral glaucoma, modifications of tension were noticeable only in the healthy eye. It is supposed that the glaucomatous eye failed to react on account of pathological adhesions. After iridectomy, opotherapy helped to keep the intra-bulbar tension low—G V

(GONADS) Genetic and clinical study of five cases of hereditary-familial eunuchoidism (Studio di genetica e di clinica sopra

cinqe casi di eunucoidismo eredo-famigliare) Furno (A), Riv di patol nerv (Firenze), 1922, 26, 245-284

Five cases of eunuchoidism in three generations in one family are described. The author's conclusions are as follows: (1) There is a form of hereditary-familial eunuchoidism, clearly distinguished from the forms of direct transmission from father to son, which necessarily are only slight spurious forms of hypogenitalism. (2) The hereditary-familial form, which is "dominant," usually mendelizes. The female sex appears to transmit the abnormality. (3) Four distinct forms of eunuchoidism are found, which can be classified as follows: (a) simple deficiency or absence of genital glands, (b) gerodermic eunuchoidism, in which the pathological hormonal influence of thyroid and hypophysis is added to congenital hypogenitalism, (c) acromegalic eunuchoidism, in which the pathological hormonal influence of the hypophysis complicates the congenital hypogenitalism, (d) eunuchoid feminilism, in which the congenital hypogenitalism is accompanied by a probable influence of heterosexual hormones from ovarian elements (endocrine hermaphroditism). (4) Pure eunuchoidism is therefore a monoglandular syndrome, the other clinical varieties are pluriglandular. (5) The gerodermic and acromegalic varieties of eunuchoidism and feminilism are not such from birth, as is the case with pure eunuchoidism, but develop during the puberal period. (6) Libido may appear, but it is tardy and does not last. (7) There is no constant finding in regard to vagotonia or sympatheticotonia in eunuchoids. (8) Grafting of cryptorchidic testes, rich in interstitial substance, is the best treatment, opotherapy gives negative results. When the grafts survive, the morphology and the psyche improve to normal, with the exception of the generative power. Even should the graft be absorbed general improvement results.—G V

(GONADS) *Dystrophies and infantilism in chronic appendicitis of children* (Distrofie ed infantilismo nelle appendiciti croniche degli adolescenti) Cignozzi (O), Riforma med (Napoli), 1922, 38, 55-58

Cignozzi reports several cases of chronic appendicitis, accompanied by infantilism and genital dystrophy in young people. After operation striking improvement of these conditions was seen.

—G V

(GONADS) *Pubertas praecox combined with hermaphroditism* Collet, Ugesk f Læger (Copenhagen), 1921, 83, 937

The author mentions a case of precocious puberty and hermaphroditism in a child, aged 1½ years, in whom a removable tumor of the adrenal cortex was found.—K H K

(GONADS) The independence of the seminal gland and the secondary sexual characters in fish (Sur l'indépendance de la glande séminale et des caractères sexuels secondaires chez les poissons étude expérimentale) Courrier (R), Compt rend Acad d sc (Par), 1922, 174, 70-72

Spermatogenetic division in the testes of the winter-stickleback is activated by heat (keeping the fish in running water at 17° C) and seminiferous ampullae are obtained having a structure completely identical with those present in the fish in summer. The seminal gland, under this treatment, qualitatively and quantitatively the same as at the mating period, does not, however, produce the appearance of secondary sexual characters, especially the special secretion of the kidney, although this organ is under the same conditions of temperature and nutrition as in summer. The two secondary sexual characters of the stickleback do not therefore react in the same fashion to the sexual hormone. The difference appears to be quantitative. A smaller amount is capable of influencing the chromatophores —A T C

(GONADS) Influence of castration on respiration, nutrition and fasting (Influence de la castration sur les échanges respiratoires, la nutrition et le jeûne) Heymans (C), J de physiol et de path gén (Par), 1921, 19, 323-331

Total castration diminishes the metabolism of the cock in normal nutrition from 20 to 30%. Partial nodular castration, although it conserves the morphological aspect of the bird, diminishes the respiratory exchange some 15%. This excess of metabolism of the normal cock over that of the castrate is considered as a secondary sexual characteristic. Fasting reduces the respiratory metabolism within 3 days to that of the castrated animal. The resistance to inanition of the cock is much lower than that of the castrate —F S H

(GONADS) Pubertas praecox in relation to tuberculous sclerosis (Krabbe (K), Ugeskr f Læger (Copenhagen), 1921, 83, 1284

- Short description of two cases of tuberculous brain sclerosis combined with pubertas praecox in boys, aged 5 years and 13 years. The cases were described in detail in L'Encéphale (Paris), 1921
—K H K.

(GONADS) Alimentary atherosclerosis in castrated animals (rabbits) Murada (K), & Katsaka (B), Nisshin Igaku, 1918, 8, 1321-1340

Alimentary atherosclerosis was more marked in castrated animals than in controls. This is attributed to the hypercholesterinemia which exists in castrated animals, which results in the

deposit of both neutral and doubly refractile fat in the walls of the vessels The anatomical changes were practically identical with those of human atherosclerosis The greater prevalence of atherosclerosis in Europeans than in Japanese is attributed to their meat diet —L G K

(GONADS) Comparative haemolysin formation in male and female rabbits Ohnara (K), Chuo Igakki Zasshi, 1918, No 276, 1387-1388

The pregnant female rabbit, and castrated females formed more hemolysin than did normal males, or non-pregnant normal females This, the author attributes to the cessation of the internal secretion of the ovaries —L G K

Radioexcitation of the GONADS (Radioeccitamento delle ghiandole sessuali) Pais (A), Riforma med (Napoli), 1921, 37, 1136

By exposure of the sexual glands to minimal doses of x-rays increase of the spermatozoa has been obtained as well as acceleration of delayed puberty with amenorrhea —G V

(GONADS) Sexual desire and internal secretion (Geschlechtstrieb und innere Sekretion) Weil (A), Deutsche med Wchnschr (Berl), 1922, 48, 188-189

Description of two cases (1) A woman of 24 with powerful muscles, strength and intelligence When she was 23 she lost some drops of blood from time to time, but she has never had a real menstruation The labia majora are small, the labia minora, large, the clitoris is small The uterus and ovary cannot be palpated She is very intelligent but has no sexual desire (2) A man of 35 without any growth of beard At 20 years he had never felt any sexual desire, but married for social reasons In the beginning of his marriage he sometimes felt sexual desire but it soon disappeared He is very tall with a typical eunuchoid habitus He has few pubic hairs and otherwise, no hairs on the trunk His larynx is defectively developed His scrotum is large, but his testicles, extremely small He is extraordinarily intelligent —J K

HYPOPHYSEAL syndrome (Syndrome hypophysaire) Achard (C) & Rouillard (J), Bull et mém Soc méd d hôp de Par, 1922, 46, 562-566

A case report with no novel data —F S H

(HYPOPHYSIS) A case of dystrophia adiposo-genitalis (Un caso di distrofia adiposo-genitale) Albertario, Pediatria, (Napoli), 1921, 29, 659

A report of a case of dystrophia adiposo-genitalis in a boy 12 years old, whose father is diabetic and whose mother has gout,

there is also tuberculosis on the mother's side No abnormality of the sella was found nor extra-hypophyseal cerebral lesions The condition followed pertussis when the child was 4 years old The author considers the case as a functional dystrophy of the hypophysis as shown by high tolerance of carbohydrates and insists on the interrelation of this condition with arthritism, diabetes and obesity Pituitary and thyroid medication improved the patient very much —G V

HYPOPHYSEAL disease Askgaard (V), Hosp-Tid (Copenhagen), 1919, 62, Neurol Soc Report, 8

A boy, 14 years old, suffered during the last year from thirst, attacks of headache and vomiting He presented an infantile character, and was somewhat adipose His genital organs were like those of a boy of 6 or 7 years Urine output was 1700-2240 cc Blood sugar was normal The symptoms pointed to pituitary disease —K H K

The morphogenesis of the HYPOPHYSIS in the tailed amphibia Atwell (W), Anat Record (Phila), 1922, 23, 8

Data given more completely elsewhere

Lethargic enccephalitis with marked polyuria HYPOPHYSEAL polyuria and pithiatric polyuria (Encéphalite léthargique avec polyurie extrême Polyurie hypophysaire et polyurie pithiatique) Benard (R), Bull et mém Soc méd d hôp de Par, 1922, 46, 553-557

Report of a case of polyuria of 17 to 22 L per day responding to pituitary treatment and psychotherapy —F S H

Two peculiar cases of tumor of the HYPOPHYSIS (Due no tevoli casi di tumori dell'ipofisi) Ceresole (G), Riforma med (Napoli), 1921, 37, 668

Radioscopy showed in one subject a tumor involving the anterior pituitary, penetrating the sphenoidal sinus, while the anterior clinoids were destroyed In the second subject, the tumor had developed posteriorly with destruction of the posterior clinoids and of the lamina quadrilatera, but without lesions of the sphenoidal sinus Radiotherapy was of no avail in the first case, but in the second, brought a great improvement in the soporous condition, the genital field, the papilla and the headaches —G V

(HYPOPHYSIS) Pituitrin in obstetrics Cleveland (C H), N Orl M & S J, 1922, 74, 701-704

A general discussion of the indications and contra-indications for the use of pituitrin Conservatism is advised —R G H

The relation of the **HYPOPHYSIS** to antibody production Cutler (E C), J Exper M (Balt), 1922, 35, 243-257

The author undertook to determine whether the hypophysis plays any part in the development of resistance to infection Guinea-pigs were employed as the experimental animals and the serum reactions of typhoid agglutination, hemagglutination and hemolysis were studied In one series of animals the hypophysis was partially removed by a special method devised for this study, after which the immunological tests were made In a second, the immune reactions were first developed, after which hypophysectomy was done, while in a third, animals were immunized, then fed continuously pituitary extract or given repeated injections and their titers subsequently determined Normal and control operative animals were used throughout None of these procedures, aiming to disturb the normal function of the hypophysis, had the slightest effect on the immunological reactions—I M

Experimental echinococcosis of the posterior lobe of the **HYPOPHYSIS** Hypophysial lesion of infundibular origin (Echinococcose expérimentale due lobe postérieur de l'hypophyse Lésion hypophysaire d'origine infundibulaire) Dévé (F), Compt rend Soc de biol (Par), 1922, 86, 95-97

Histological description of an echinococcus cyst of the hypophysis (posterior lobe) previously noted (Compt rend Soc de biol April 23, 1921) —T C B

Pituitary nanism with tumor in the **HYPOPHYSEAL** region Faber (K), Ugesk f Læger (Copenhagen), 1919, 81, 1956-1962

History of a man aged 17 years with nanism, genital dystrophy, polyuria and thirst, optic atrophy and contraction of the visual fields On the right side was both a nasal and temporal defect, on the left a small nasal defect Radiography showed the sella turcica normal, but above this there was an intense shadow, probably from a calcified tumour The disturbances of the visual fields pointed to a process in the chiasma region Hypophysine treatment was without effect —K H K

Variations of the blood pressure following injection of **HYPOPHYSIN** in different morbid conditions of infants (Le variazioni della pressione sanguigna in seguito ad iniezione di ipofisina in vari stati morbosi dell'infanzia) Fabris (S), Pediatria (Napoli), 1921, 29, 548-557

The researches have been made in children from a few months to 12 years old One cc of "endo-ipofisina" of the Ist Sierotherp Milanese was injected, the effect was studied on 52 children It was found that the variations of pressure resulted in every case in

from 10 to 15 minutes after the injection. All children similarly affected offered an identical type of reaction, no matter what their age. The change of pressure was never more than 1 cm (Pachon). The maximum and minimum variations ordinarily ran parallel, but in cases of bronco-pneumonia decrease of the maximum synchronized with a rise of the minimum pressure. The reaction lasted, on the average, 75 minutes, after which the pressure became normal. In most cases the minimum became normal before the maximum. In 13 cases the increase was preceded by a lowering (almost all cases of latent tuberculosis, nephritis or diabetes insipidus). In 15, steady increase of pressure was shown after the injection (scrofula, exudative diathesis, tracheo-bronchial adenopathy, cerebral tuberculoma). In 22, a paradoxical reaction was noted, namely, a steady, slow decreasing of the pressure (mitral stenosis, polyuria, bronco-pneumonia, kalazar, tuberculous peritonitis, pleuro-peritonitis, lymphatism). The author feels that an extension of such observations may lead to important diagnostic criteria, both as regards organic lesions and hormone balance.—G V

(HYPOPHYSIS) Acromegaly from late hereditary lues (Sindrome acromegalico por heredo lues tardia) Gazzolo (J J), Prensa méd argentina (Buenos Aires), 1921, 8, 259

A 28 year old patient complained of headaches and dizziness. The hands and feet were slightly large, the features somewhat acromegalic. Hereditary syphilis is regarded as the causal factor because of a positive Wassermann reaction, pigmented scars of the limbs, and slight anisocoria. Amelioration followed mercurial treatment. The skull was not radiographed.—B A H

Clinical study of hypertrophy of the HYPOPHYSIS during pregnancy (Klinischer Beitrag zur Schwangerschaftshypertrophie der Hypophyse) Jung (P), Schweiz med Wchnschr, 1922, 52, 61-62

Jung points out that the diagnosis of enlargement of the hypophysis during pregnancy largely depends upon the x-ray picture. Usually a marked enlargement of the sella turcica occurs, characterized by a distinct outward curve. The hypophyseal hyperplasia is rarely so marked as to induce a clinically perceptible condition. Two pertinent cases are cited from the literature and these are followed by a detailed description of the author's case. The author believes that in such cases a primary disease of the hypophysis exists, simulating an adenoma. During pregnancy this hypophyseal condition acquires a certain growth stimulus which disappears after the termination of pregnancy, leading to the retrogression of the hypertrophy. The pressure on the optic chiasm is decreased and the visual disturbances diminish.—C P McC

Researches on the normal and pathological structure of the pharyngeal HYPOPHYSIS (Ricerche sulla struttura normale e patologica

della ipofisi faringea) Lunghetti (B) R Accad d fisiocritici in Siena, 1920, abst, Pathologica (Genova), 1922, 13, 58

The pharyngeal hypophysis, which is almost constant in man, is otherwise seen among vertebrates only in some birds (gallinacea) and carnivora. It is formed, especially in man, of glandular tissue, structurally similar to that of the pars tuberalis of the hypophysis. It is supposed that the pharyngeal hypophysis, though within narrower limits, has a function similar to that of the anterior lobe, and it can be inferred that, owing to the presence of parenchymal cords, pavement epithelium and vacuolizations, it may give origin to blastomata. In inflammations of the pharynx as well as of the pharyngeal tonsil it may undergo alterations, as is the case with the anterior lobe. This can be explained by the strict relations (topographic, vascular) with the pharyngeal tonsil and mucosa. Owing to this it may show hyperemia, connective septa thickened or infiltrated with leukocytes, and various alterations of the parenchyma. The anterior lobe, also, may undergo congestion and accentuated fluctuations in its chromophil elements, colloid and enclosed cells. On account of the frequency of such alterations in several diseases the author is in doubt whether the anterior lobe should be incriminated in cases giving pituitary symptoms without thoroughly excluding the possibility of the pharyngeal hypophysis being at fault.—G V

HYPOPHYSIS and ADRENAL changes in fetal pseudo-hermaphroditism (Sulla presenza di cellule simil-gravidiche nell'ipofisi, di formazioni ghiandoliformi nella corteccia surrenale e di altri fatti degni feto pseudoermafrodita) Pelligrini (R), Riforma med (Napoli), 1917, 32, 1089-1123

Reference verified from Index Medicus

Hirschsprung's disease and HYPOPHYSEAL nanism (Morba di Hirschsprung e nanismo ipofisario) Samaja, Pediatria (Napoli), 1922, 30, 35-36

Report of a case of nanism in a girl of 20, whose mother's stature is below normal. The sella turcica of the patient is very small and the anterior and posterior clinoids joined. She has enlarged esophagus, megacolon and megarectum. Samaja advances the hypothesis that if the post-pituitary constantly secretes pituitrin it should exert a steady influence on the contraction of the smooth fibres of the intestine. Through deficiency of this action, once a congenital hypertrophy of the circular fibres is given at a certain point, dilatation through stasis may occur and a consequent hypertrophy of the longitudinal fibres above the obstacle.—G V

Tumor of the HYPOPHYSIS presenting clinical manifestations very similar to retrobulbar neuritis Tone (S), Chuo Kanka Iho, 13, No 3, abst, Jap Med World (Tokyo), 1921, 1, 20

The author observed a very interesting case of pituitary tumor in a male, 45 years old, who complained of difficulty of vision in both eyes —R G B

Anatomical modifications of the HYPOPHYSIS after removal of the thyroid (*Sulle modificazioni anatomiche dell'ipofisi degli animali stiroidati*) Vallillo (G), Boll d Ist steroterap Milanese, 1920, 213-223, abst, Pathologica (Genova), 1922, 13, 55

The histological observations on the prehypophyseal parenchyma of goats and horses previously deprived of the thyroid show modifications, on the whole equal in all cases. These modifications are characterized by increase of the eosinophil cells, or by their regressive alterations. The presence of new elements determines the increase in the weight of the gland. There was found no relation between the condition of the hypophysis and the length of time elapsing after the removal of the thyroid. It is concluded that the eosinophil tissue increases through a process of restitution, which, as happens in analogous cases, may go beyond the normal. This hypothesis explains the macroscopic and the microscopic findings. In the animals discussed it has not been found that the combined action of the regressive and progressive phenomena on the hypophyseal parenchyma causes hypertrophy —G V

Pathological findings in the HYPOPHYSIS and PARATHYROID glands Harbitz, Forh med Selsk i Kristiana, 1916, 20-25

Reference verified from Index Medicus

Clinical case of pathological dissociation between the two lobes of the HYPOPHYSIS (*Caso clinico di dissociazione patologica fra i due lobe dell'ipofisi*) Samaja (N), Riv sper di Freniat (Reggio-Emilia), 1920, 44, 540-564, abst Pathologica (Genova), 1922, 13, 56

The author found a case of moderate gigantism (without symptoms of eunuchoidism or other endocrine insufficiency) complete at 16 years of age. The subject showed an exaggerated tolerance for carbohydrates and relative oliguria. The earlier manifestation was one of hyperfunction of the anterior lobe, the second, of hypofunction of the posterior lobe. The hypertrophy of the anterior lobe in the restricted space apparently caused first irritation of the posterior lobe with subsequent pressure atrophy. Such a functional dissociation has been observed, even if not explained, in regard to acromegaly. In a case of Falta's the alimentary glycosuria was positive in the beginning but later, negative. W Schlesinger and Borchardt published a similar case and recently Cushing has discussed analogous cases. In Borchardt's case the diabetes lasted 5 years, but afterward no glycosuria could be provoked with 150 gm of glucose. Polyuria is also a transitory phenomenon in acromegaly. In the

first period, therefore, the proliferative process of the anterior lobe, which causes acromegaly, irritates the posterior lobe, producing glycosuria and spontaneous diabetes, afterward the posterior lobe atrophies and the exaggerated tolerance of carbohydrates follows alimentary glycosuria—G V

The importance of the **HYPOPHYSIS** in the etiology of diabetes mellitus (Ueber die Bedeutung der Hypophyse in der Pathogenese des Diabetes mellitus) Vernon (O), Zentralbl f allg Path u path Anat (Jena), 1921, 31, 521-531

This work, from the Pathological Institute of the University of Jena, is largely a speculation, to some extent based on the anatomical studies of six cases of diabetes mellitus. The absence of anatomical lesions in the islands of Langerhans in many diabetics is noted, also the vast literature involving other glands of internal secretion with sugar tolerance and metastasis. Of these, he selects the hypophysis. Experimental workers have reported glycosurias accompanying injury or removal of the anterior lobe and the increased tolerance for sugar associated with injury or removal of the posterior lobe. Lowered tolerance and glycosuria is frequently seen in acromegaly. "Heute wissen wir, dass diese Erkrankung (Akromegalie) auf einer Ueberfunktion des Hypophysenvorderlappens beruht" (!) No systematic anatomical studies on the hypophysis in diabetes have previously been recorded. Six cases, with autopsy findings are reported, in three of which no lesions of the pancreas or islands of Langerhans could be found. One that developed, following a fall from a scaffold, was clinically diagnosed as traumatic diabetes, and autopsy showed necrosis of the stalk of the pituitary. The second was a long standing, mild case of exophthalmic goitre in which there was moderate enlargement of the anterior lobe of the hypophysis (eosinophilic type). A third was a case of carcinoma of the lung (bronchial type), in which the posterior lobe of the hypophysis was nearly destroyed by metastasis. While the experimental work does not entirely convince one that there is a relation between diabetes and the hypophysis, it seems to show that hyperfunctioning of the anterior lobe and stimulation of the posterior lobe can cause glycosuria. There are cases of diabetes mellitus in which the pathological findings suggest hypophyseal origin, as in the case with traumatic necrosis and tumor destruction of the normal connection of the hypophysis with the brain—D M

Case of true **INFANTILISM** Klein (J), Ugeskr f Læger (Copenhagen), 1919, 81, 899-908

A woman, aged 25 years, showed a typically infantile aspect height 124 cm, weight 35 kg, no development of mammae, no pubic or axillary hair, open epiphyseal lines (radioscopically), very infantile psyche, slight lymphocytosis. There was a slightly deform-

ing tuberculous spondylitis The case was considered by the author
as one of true infantilism There were no other endocrine signs
—K H K

(LIVER) The cardio-accelerator agent produced by hepatic stimulation Cannon (W B) & Griffith (F R), *Am J Physiol* (Balt), 1922, 59, 480

The accelerator effect on the denervated heart of stimulating the hepatic nerves is not due to the failure of the liver to protect the heart from substances absorbed from the intestinal canal, for blood drawn from the hepatic veins during stimulation will accelerate the heart when injected into the inferior vena cava. As a rule the effect is most marked during the digestion of meat. It seems probable that a substance of special and unknown nature is discharged into the blood stream when the hepatic nerves are excited —T C B

Variations of the hematic reaction to LYMPHOGANGLINE (*Sopra alcune variazioni del reperto ematico prodotte dalla Linfoganglina con speciale riguardo alla eosinofilia*) Mazzarella (A), *Riforma med* (Napoli), 1921, 37, 1103-1104

The article is a preliminary note on the action of lymphatic ganglia extract, which increases the number of the white corpuscles, but modifies the formula by inducing mononucleosis and eosinophilia. The eosinophilia differs from that produced by serum or excitation of the vagus (pilocarpin). The experiments are said to confirm the observations of Marfori and Christoni that lymphogangline has a hormonal action antagonistic to adrenalin —G V

LIPODYSTROPHY Askgaard (V), *Hosp-Tid* (Copenhagen), 1921, 64, *Neurol Soc Report*, 18-19

A woman, aged 33, showed very marked emaciation of the face and thorax, contrasting strongly with very voluminous nates, hips and legs —K H K

Two cases of MACROGENITOSOMIA from internal hydrocephalus with a note on the differential diagnosis of hydrocephalus and on the question of repeated ventricular puncture (*Zwei Falle von Makrogenitosomia ex Hydrocephalo interno, zugleich ein Beitrag zur Differentialdiagnose des Hydrocephalus und zur Frage der wiederholten Ventrikelpunktion*) Gabschuss (G), *Monatschr, f Kinderh* (Leipz & Wien), 1922, 22, 574-586

Two cases of macrogenitosomia praecox are reported in girls, aged 9 and 9½ years, respectively. In both there was premature development of the external genitalia and the breasts, but menstruation had not appeared. Neurological disturbances were present in both, they were relieved by trepaning and repeated ventricular punctures. There was no evidence of tumor and the author reports both

children as having internal hydrocephalus. He believes this to be responsible for the general bodily changes, perhaps by pressure on the hypophysis or pineal with resultant endocrine disturbance

—C H G

MONGOLISM of possibly abortive form in congenital heart disease

Krabbe (K H), *Bibliot f Læger* (Copenhagen), 1919, 3, 70-76

The author describes a case of congenital heart disease which showed some slight signs of mongolism, namely, epicanthus, deviation of the 5th finger, retarded physical development, hypotonia, and slight retardation of ossification. The patient did not show such marked idiocy as that of the ordinary mongolian type. The existence of abortive forms of mongolism should be considered, especially in cases of congenital heart disease. In accordance with most modern authors, Krabbe considers mongolism as due to a general deficient fetal development, not as an endocrine disease —K H K

The rôle of the LUTEIN cells of the OVARY in certain uterine hemorrhages (Du rôle des cellules lutéiniques de l'ovaire dans certaines hémorragies utérines) DeRonville (G) & Sappey (P), *Gynéc et obst* (Paris), 1922, 5, 1-38

Clinical and histological report of 12 cases of ovarian and menstrual disturbances. The conclusions are that menstruation is due to the internal secretion of the ovary formed by the lutein cells, either the interstitial cells of the theca interna or the cells of the corpus luteum. Hyperfunction of these structures produces pathological hemorrhage. Amenorrhea is the result of hypofunction

—F S H

(MAMMA) Lactation and menstruation (Laktation und Menstruation) Engel (S), *Monatschr f Kinderh* (Leipz & Wien), 1922, 22, 545-551

The author discusses the prevalent views as to the effect of menstruation on lactation. He also presents curves showing the total daily milk secretion in two wet nurses. No change in the form of these curves occurred with the reappearance of menstruation. Engel accepts the view that the reappearance of the menstrual flow follows the failure of the mammary secretion and is not the cause of the failure as is commonly supposed —C H G

The OVARY and the endocrinologist Frank (R T), *J Am M Ass* (Chicago), 1922, 78, 181-185

The development of the sexual duct systems (Wolffian and Mullerian ducts) and of the secondary sex characters are qualitatively and quantitatively governed by the sex glands. The transformation of the infantile genital tract, inclusive of the secondary sex characters, to the adult stage results from a quantitative increase in

ovarian secretion Menstruation signifies the abortion of an unimpregnated ovum The "interstitial gland," as emphasized by Meyer, *does not exist in the human female* Frank calls attention to the work of Iscovesco, Herrmann and others on the lipoidal bodies contained in corpus luteum, which produce uterine hyperemia and hyperplasia Hypoplasia of the female duct system (vagina, uterus, tubes) results from insufficient ovarian action He, contrary to many investigators, considers other factors, such as the pituitary, of no importance in this connection He laments the fact that today we have no better ovarian extract on the market than we had in 1910 and considers the "degreased" or "defatted" commercial preparations pharmacologically inert —E N

The CORPUS LUTEUM (Contribuzione allo studio del corpo luteo) Galfami, *Riforma med* (Napoli), 1921, 37, 1136

No original data It is denied that the corpus luteum has any influence in determining extrauterine pregnancy —G V

(OVARY) Therapy and pathogenesis of osteomalacia (Contributo clinico alla terapia e patogenesi dell'osteomalacia) Gentili (G), *Riforma med* (Napoli), 1922, 38, 97-98

Report of two cases of osteomalacia during and following pregnancy, which have been treated with "Ovarial" (Calcium phosphate and ovarian extract) From the very satisfactory results obtained in both cases Gentili infers that osteomalacia is due, not to hyperfunction of the ovaries, but to dysfunction of these glands The "Ovarial" was given in doses of from 20 to 30 drops before each meal for one or one and a half months, followed by a rest period of fifteen days —G V

Swelling of the MAMMA in new born infants (Über die Milchdrüsen-schwellung bei Neugeborenen Zugleich über extramedellare Blutbildung) Gruber (G B), *Ztschr f Kinderh* (Berlin), 1921, 30, 336-362

A well illustrated study of the histological changes associated with the swelling of the mammary glands in new born infants Not of immediate endocrine interest —C H G

(OVARY) Morphological and physiological studies on the musculature of the mature Graafian follicle of the sow Guttmacher (M S) & Guttmacher (A F), *Johns Hopkins Hosp Bull* (Balt), 1921, 32, 394-399

The ovaries were promptly immersed in Bouin's fluid After fixation, and the usual paraffin embedding technique, the tissue was sectioned at from 3.3 to 5 micra The sections were then stained in haematoxylin with iron alum as a mordant After decolorization they were subjected to the Van Gieson technique for the differen-

tiation of smooth muscle and connective tissue fibers For the study of the nerve supply, good results were obtained by Ehrlich's methylene blue staining, following the modifications of J G Wilson The method is fully described The authors found an abundance of smooth muscle cells in the theca externa Autonomic nerves with typical motor endings occur in juxtaposition to these cells The musculature of the ovary and its follicles has a double innervation, the true sympathetics acting as inhibitory and the parasympathetics as excitatory nerves The innervation is similar to that of the intestinal musculature The authors were not able to demonstrate rupture of the follicles by producing contractions of the muscle fibres, but they feel that they have demonstrated that rupture of the follicle is not produced solely by an increase in the arterial tension of the follicular vessels—E M

CORPUS LUTEUM extract in the treatment of the vomiting of pregnancy King (E L), J Am M Ass (Chicago), 1922, 78, 484-486

A report of 48 cases of vomiting of pregnancy Of these, 12 were treated with extract of corpus luteum, ten received corpus luteum only, while 2 received ovarian extract, also Nine were treated with ovarian extract alone Twenty-eight received the usual treatment of sedatives, gastric lavage, colonic irrigations of sodium bicarbonate, forced fluids, glucose, etc, two of this group were also given horse serum, with negative results From this experience, the author cannot share Hirst's enthusiasm over the corpus luteum treatment True, some mild cases were cured, but the same may be said of any other line of treatment He criticizes adversely the theory on which Hirst bases this form of treatment—E N

MENSTRUATION and the swelling of other organs (*Menstruation und Wellenbewegung*) Labhardt (A) & Hüssy (P), Ztschr f Geburtsh u Gynäk (Stuttg), 1922, 84, 715-741

Biological experiments on guinea-pigs demonstrated an extra-genital swelling of various organs synchronous with the sexual cycle The high point of this swelling occurs in the pre-gravid state or the beginning of menstruation Its origin is in the monthly preparation for pregnancy Its first phase is anabolic and is necessary for the increased activity of the organism This is followed by a catabolic phase, if the ovum is not fertilized, and a decrease in activity of the whole body Menstruation, as such, is only a symptom of a general swelling The important phase is the pre-gravid A good review of current data is included—F S H

Hypertrophy of fragments of the OVARY in partial castration (*Sur l'hypertrophie des fragments ovariens dans la castration partielle*) Lipschutz (A), Wagner (C), & Tamm (R), Compt rend Soc de biol (Par), 1922, 86, 240-242

Carmichael and Marshall have shown that ovarian fragments in the rabbit undergo remarkable hypertrophy. The authors in a series of experiments have verified this. The hypertrophy is caused exclusively by the entering into follicular development of a relatively large number of ovules.—T C B

Relation of corpus luteum to menstruation and pregnancy Mackenzie (W R), Brit M J (Lond), 1922, i, 343-344

A report of five operative cases which lead the author to conclude that injury to either a true or false corpus luteum will simulate a ruptured extrauterine gestation, that injury to a true corpus luteum will bring on an abortion, and that rupture of a false corpus luteum will bring on menstruation and its accompanying ovulation

—E N

The antagonistic action of the OVARY on ADRENALIN glycosuria Mochizuki (K), Nikon Fujinka Gakkwai Zasshi, 10, No 9, abst, Jap Med World (Tokyo), 1922, 2, 46

The author concludes that the ovary and adrenal glands act antagonistically on carbohydrate metabolism.—R G B

(OVARY) The change in blood sugar after castration (I Communication) Nakanarinmi (S), Keio Igaku, 1, No 7, abst, Jap Med World (Tokyo), 1922, 2, 15

The author estimated the blood sugar in young and old female rabbits whose ovaries had been extirpated. There was a marked rise in blood sugar which was hastened by the injection of adrenalin hydrochloride. An injection of ovarian extract rapidly brought the hyperglycemia approximately to normal. When a combination of adrenalin and various extracts was injected into a castrated rabbit with blood sugar changes and into a normal rabbit, the same changes were obtained in both. This would imply that the accelerated chromophilic action could be depressed by the administration of ovarian extract.—R G B

(OVARY) Chronological and causal relations between labor, ovulation and menstruation (Zeitliche und kausale Beziehungen zwischen Geburt, Ovulation und Menstruation) Novak (J), Centralbl f Gynäk (Leipz), 1921, 45, 1697-1699

The author presents a very interesting hypothesis as to the cause of the onset of labor. He calls attention to the striking fact that the first menstrual period in the non-lactating woman as a rule makes its appearance six weeks after labor. This would indicate that labor occurs at the time of an ovulation, for the latter is known to take place about midway between the periods. He believes that ovulation during pregnancy is inhibited by the corpus luteum and later by the placenta, but that this restraining influence is removed

toward the end of pregnancy He mentions various clinical facts in support of his hypothesis, which would be considerably strengthened, as he himself says, were it possible to demonstrate recently ruptured follicles in the ovaries of women dying in labor —E N

MENSTRUATION and its anomalies A critical compilation of the literature of 1915 to 1918 (*Der Menstruationszyklus und seine Anomalien Das Ergebnis der kritisch zusammengestellten Gesamtliteratur der Jahre 1915, 1916, 1917, 1918*) Schroeder (R), *Monatschr f Geburtsh u Gynaek (Berl)*, 1920, 53, 207-251

This is an excellent and quite exhaustive review of the general subject by one who has himself been one of the most industrious workers in the field The subject is considered under seven headings, viz (1) The anatomy of the menstrual cycle, (2) the cause of the menstrual cycle, (3) the physiology of the menstrual cycle, (4) too early and too late menstruation, vicarious menstruation, results of castration, climacterium, (5) amenorrhea, (6) dysmenorrhea, (7) meno- and metro-rrhagia —E N

The influence of **CORPUS LUTEUM** extract on erythropoiesis in artificially anemic rabbits (*Ueber den Einfluss von Corpus Luteum-Extrakt auf die Erythropoese bei künstlich anamisierten Kaninchen*) Rothlin (E), *Arch f d ges Physiol (Berl)*, 1922, 193, 102-108

Anemia was produced by bleeding Subcutaneous injection of extract had no effect Feeding desiccated corpus luteum had no effect on females, on males there appeared to be a favorable effect There was no definite alteration in the color-index —A T C

OVARIAN lipoids (*Sui lipoidi contenuti nell'ovaio*) Serono (C) & Palozzi (A), *Folia Med (Napoli)*, 1916, 2, 34-41

Reference verified from Index Medicus

Internal secretion of the **OVARY** and osteomalacia (*Cellule a secrezione interna dell'ovaia ed osteomalacia*) Spirito (F), *Riforma med (Napoli)* 1921, 37, 1137

From his personal observations the author objects to the statement of Wallart that hypertrophy of the interstitial ovarian tissue may be a factor in osteomalacia —G V

Lipoid metabolism of CORPUS LUTEUM (*Metabolismo lipoido del corpo luteo*) Tricomi (E), *Riforma med (Napoli)*, 1921, 37, 762

According to a series of observations of Tricomi on the corpus luteum of the cow it appears that the amount of fat increases from the first days to the fifth month, then it decreases, to increase again

from the seventh month on The fat is nearly all lipoid the first two months, its amount does not increase with the increase of fat, but diminishes after the third month to almost total disappearance at the end of pregnancy—G V

Experimental researches on the effect of removal of the OVARY, ADRENALS and THYROID during pregnancy (*Ricerche sperimentali intorno all'asportazione dell'ovaia, surrene, tiroide rispetto all'andamento della gravidanza*) Sirtori (C), Riv crit di med (Firenze), 1919, 20, 358

Bilateral ovariectomy in the first days of pregnancy as well as destruction of corpus luteum (by chemical means, in situ) always leads to abortion During the first half of pregnancy ovariectomy nearly always has the same effect, while within a few days of conception, destruction of corpus luteum "in situ" allows pregnancy to proceed In the second half of gestation neither type of interference causes abortion Bilateral ovariectomy and subsequent grafting of ovaries into the peritoneum does not interrupt the pregnancy Unilateral adrenal ablation in the first days induces abortion, while bilateral ablation causes abortion on the first or second day and death within three days At a later period unilateral adrenal destruction proves harmless, but should both ovaries be removed in addition, death occurs before abortion Partial thyroidectomy in the first days leads to abortion, while no effect results in a later period The author claims that the hormones of the foetus may act on the mother—G V

Studies of the centrally conditioned changes in blood sugar and the influence of the internal secretion of the OVARY on this reaction, together with a new proof of the internal secretion of the ovary (*Beitrage zu Physiologie der Drusen LII Untersuchungen uber zentral bedingte Veranderung des Blutzuckergehaltes und uber den Einfluss des inneren Sekretes des Ovariums auf diese Reaktion zugleich ein neuer Nachweis der inneren Sekretion des Ovariums*) Takakusu (S), Biochem Ztschr (Berl), 1922, 128, 1-31

The blood sugar changes were studied on normal and castrated female rabbits after the injection of theobromine sodium salicylate It was found that the hyperglycemia produced as the result of the administration of this compound became less as the interval between the loss of the ovaries and the test increased The drug hyperglycemia is supposed to be centrally conditioned because the sensitivity of certain parts of the central nervous system is reduced after loss of the ovarian hormone When a castrated rabbit is parabiotically joined with a normal animal the reaction to the drug is increased, but it is decreased after disjunction This is taken as a proof of a circulating ovarian hormone The removal of the ovaries results in marked atrophy of the uterus and vagina The decrease in the

hyperglycemia induced by the drug after ovariectomy is specific for the sex, since testicular extirpation is not followed by a similar phenomenon. Castration does not change the reaction of rabbits to heat puncture —F S H

Precocious MENSTRUATION and mammary organotherapy (Mestruazioni precoci e opterapia mammaria) Tronconi (S), Morgagni, 1921, —, —, No 27, Abst, Terapia (Milano), 1921, 11, 18

Report of a six year old girl, whose mother is affected with goiter. The girl shows precocious puberal development and has menstruated. To stop a flow, which was rendering the patient anemic, the usual medication was of no avail. Mammary gland tablets were given with satisfactory result. The author compares this case with that of an infant of 16 months whose vaginal flow (not cyclic) was due to an ovarian tumor, in this case neither pituitary nor mammary gland had any effect. The author insists on the importance of mammary therapy for diagnostic as well as for therapeutic purposes —G V

Lipoids in the human OVARY (Lipoide im Menschlichen Ovarium) Weishaupt (E), Monatschr f Geburtsh u Gynaek (Berl), 1922, 56, 276-282

A histological study of the lipoids of ovaries from man, guinea-pigs, rabbits and one rat —F S H

The significance of the CORPUS LUTEUM in connection with Fraenkel's theory Yochelman (T), Mag Lond (Roy Free Hosp) School Med f Women (Lond), 1916, 11, 41-47

Reference verified from Index Medicus

DYSMENORRHEA Young (J V D), N York M J, 1921, 114, 395-397

Of no endocrine interest, except for a highly speculative hypothesis as to the causation of dysmenorrhea —E N

The internal secretion of the PANCREAS Banting (F G), Best (C H) & Macleod (J J R), Am J Physiol (Balt), 1922, 59, 479

A neutral or faintly acid extract of the pancreas, degenerated after duct ligation, was prepared, and its effect on pancreatic diabetes investigated. Ten weeks after ligation the gland was removed and extracted with ice-cold Ringer's solution. Injection of this extract invariably caused a marked reduction of sugar in the blood and urine. Extracts of liver, spleen and boiled pancreas had no effect. Subcutaneous injections had a less rapid but more sustained effect than intravenous —T C B

Internal secretion of the PANCREAS in pregnancy (*Ricerca istologica e fisiopatologica sulla secrezione interne del pancreas in gravidanza*) Falco (A), Ann di ostet (Milano), 1916, 1, 1-16

Reference verified from Index Medicus

Acute hemorrhagic PANCREATITIS Henrichsen (J), Hosp-Tid (Copenhagen), 1919, 62, 353-360

A woman, 38 years old, showed acute peritoneal symptoms, resembling those in peritonitis of perforation. The existence of severe glucosuria, however, pointed to pancreatic disease. Laparotomy was performed, but the result was fatal after 3 weeks. Autopsy confirmed the diagnosis acute hemorrhagic pancreatitis.—K H K

The rôle of the PANCREAS in assimilation Paulesco (N C), Arch internat de physiol (Liège & Par), 1921, 17, 85-109

The injection of a pancreatic extract into the jugular vein of a depancreatized dog may produce a transitory diminution or even suppression of the hyperglucemia, which may be followed by a hypoglycemia and the transitory diminution or suppression of the glucosuria. Moreover a decrease in the blood and urinary urea and acetone is observed. This effect begins immediately after the injection, reaches its maximum in about 2 hours, and persists for about 12 hours. It varies with the amount of pancreas used in preparing the extract. When a pancreatic extract is similarly injected into a normal dog there occurs a decrease in the blood sugar and blood urea as well as in the urinary urea. The intravenous injection of physiological serum, or of organs other than the pancreas, such as the spleen, or into the spinal canal of Na nucleinate which produces fever, fails to bring about the results described above.

—Chem Abst, 16, 580

Relation between the PANCREAS and the eyes (*Rapporti fra pancreas ed occhio*) Rentano (D), Folia Med (Napoli), 1916, 2, 319-347

Reference verified from Index Medicus

Further examinations of the PINEAL gland in mammals Krabbe (K H), Det kongelige danske videnskabernes selskabs biologiske meddelelser (Copenhagen), 1921 (III), 7, 1-30 (Résumé in French)

The author, who formerly has described the pineal gland embryologically and histologically in a series of mammals, has continued these examinations in *Echidna*, *Didelphys*, *Onychogale*, *Tamandua*, *Myrmecophaga*, lemur and *Nycticebus*, and in fetuses of *Lobodon* and *Leptonychotes*. In *Echidna* the structure is like that in many other mammals, especially *Chiroptera* and *Insectivora*. In

marsupials there are two different types, in *Didelphys* the organ is very primitive, in *Hypsirrymnus*, well developed. In *Elephas* the pineal is small and shows a follicular structure, otherwise not found in mammals. In *Tamandua*, *Myrmecophaga* and *Choloepus* the organ is absolutely missing as it is in *Dasypus*. The pineal in the higher apes resembles in some cases that of the marsupials, in others that of the lower apes. The embryological examinations in seals confirms what the author has found before in *Phoca* embryos. On the whole, the author has found a relative uniformity of the pineal in *Echidna*, some marsupials and insectivores, the higher and some of the lower apes. This type shows a rounded, slightly flattened or slightly oval form. The organ consists of uniform cells with rounded nuclei and scanty protoplasm, without discernable cell boundaries (pineal cells). Between the pineal cells are found a smaller number of glia-cells. The organ is ordinarily well vascularized. From this type the organ deviates in rodents, in which it is very long and thin, in seals, in which it is enormously vascularized, in horses, pigs, goats and men, in which there is a great deal of connective tissue, in ungulates, in which there are enormous glia, in men and higher apes in which there are many nervous elements. It is rudimentary in edentates and very small in whales and elephants.—K H K

The relation of PARATHYROID tetany to intestinal bacteria
 Dragstedt (L R), *Am J Physiol* (Balt), 1922, 59, 483

There is considerable evidence that certain types of tetany are associated with gastro-intestinal disturbances. This may be a toxemia due to putrefactive bacteria. Depending on the degree to which an aciduric or fermentative flora can be maintained, the toxemia can be prevented. An aciduric intestinal flora was produced in six young dogs by a diet of bread and milk, and milk ad libitum plus 25 gms of lactose daily. The animals lived for ten days after parathyroidectomy, and at no time developed tetany. In a series of ten adult dogs an aciduric intestinal flora was maintained by a diet of boiled rice, beef heart and lactose. Parathyroidectomy was then done, and the feeding continued. Corresponding to the degree to which an aciduric flora could be maintained, tetany was prevented. The experiments indicate a direct relation between parathyroid tetany and intestinal intoxication and lend support to the view that the function of the parathyroids is in part the removal or neutralization of toxic substances in the blood." As the animals died even when protected from tetany, the latter symptoms may be but a part of a profound metabolic derangement.—T C B

Treatment of paralysis agitans by transplantation of animal PARATHYROIDES (Beeinflussung der Paralysis agitans durch Ueerpflanzung von tierischer Nebenschilddrüse) Jakob (A), *Deutsche med Wchnschr* (Berl), 1922, 48, 113

Kuhl has stated that grafting a parathyroid may have a splendid effect in Parkinson's disease, but the same effect is obtained by systematic exercises. The disease is not due to hypoparathyroidism, but to unknown defects of the corpus striatum and the pallidum

—J K

(PARATHYROIDS) Tetanoid neuroses. Levison (P), Ugeskr f Læger (Copenhagen), 1921, 83, 1259-1268

The author gives a short description of 7 cases, which he considers as "formes frustes" of tetany. Nervousness, paresthesia in fingers and toes, slight loss of hair and slight Trousseau's and Chvostek's phenomena were observed. Treatment with calcium was followed by marked improvement.—K H K

(PARATHYROIDS) Clinical studies on tetany (Klinische Studien zur Tetanie). Melchoir (E), Mitt a d Grenzgeb Med u Chir (Jena), 1921, 34, 400-436

The parathyroids play an important part in the pathogenesis of tetany. Calcium metabolism is changed in this disease as well as in rickets and in osteomalacia, and pathological changes have been found in the parathyroids in rickets and osteomalacia. During pregnancy the nervous irritability is generally increased, the parathyroids get more blood and show an increased number of chromophil cells, while the body loses calcium. From these facts it can be seen that a relation between osteomalacia, rickets and tetany is probable, this is in accordance with the author's statement of two years ago (Berl klin Wchnschr, 1919, p 837) that the large number of cases of osteomalacia after the war would probably be accompanied by a large number of cases of tetany. The number of cases of postoperative tetany has markedly increased during the last years. One would be inclined to believe that this is due to a change in the technic of strumectomy (strumectomy totalis, ligation of the four arteries), but the author proves that in clinics where this technic is not used, more cases of tetany are also seen than before the war. It is much more probable that feeding during and after the war is the chief cause of the high number of cases. The administration of calcium lactate and parathyroid tablets sometimes has a good effect. This treatment should be tried before parathyroid transplantation because this will not always give good results. Another important point in tetany is that spasms are not always the cause of death. In postoperative and in spontaneous tetany spasms may disappear after treatment, but the patients die in coma parathyreopriva. It is possible that in some of these cases tetany of the heart, as described by Ibrahim, is the cause of death, but in others, an intoxication may be responsible for the coma. There have been cases in experimental tetany where no spasms occurred but where the patients or the animals gradually became dull and died in coma, during which the

facialis and Trousseau's symptoms were positive The abdominal organs may also show tetanic symptoms Tetany of the bladder has repeatedly been described, spasms of the stomach (x-rays of which are published in this article) are seen, though not frequently An attack of cholelithiasis has been regularly compared with an attack of tetany Tetany may also be caused by stenosis of the pylorus, lues, peritonitis or appendicitis —J K

Hyperplasia of the PARATHYROID glands in rickets Minor (J) & Pappenheimer (A M), Proc N York Path Soc (N Y), 1921, 21, 98-102

Published elsewhere

The significance of the PLACENTA, particularly the trophoblast, for the duration of pregnancy and the onset of labor (Die Bedeutung der Plazenta, insbesondere des Trophoblastes, für die Schwangerschaftsdauer, und den Geburtseintritt) de Snoo (K), Monatschr f Geburtsh u Gynaek (Berl), 1922, 57, 1-26

Report of several cases in which desiccated placenta was administered in various amounts The author concludes that the internal secretory function of the placenta rests in the trophoblast, because its origin and development is so closely associated with the growth of the fertilized ovum and its morphological alterations Since the article is mainly speculative the details are unnecessary

—F S H

Effect of PROSTATECTOMY on integration of muscular movements of the white rat Macht (D I) & Ulrich (J L), Am J Physiol (Balt), 1922, 59, 482

A study of the effect of prostatectomy on muscular coordination and efficiency by means of the "rope problem" White rats were trained to cross a room on a tightly stretched rope, starting from a platform at one end, and going to a platform containing food at the other end At first they could not cross, but after repeated trials learned to do so rapidly, and without slipping off After training there was a marked improvement in strength and tonus of the entire musculature Two sets of experiments are described In the first the rats were trained and then prostatectomized After recovery they were quickly retrained, and no change in muscular integration was apparent In the second group the rats were prostatectomized after a few trials on the rope, and after recovery training was again begun It was noticed that this second group learned very poorly, compared to the first group, and even after a much longer period they could not run over the rope in perfect fashion Progress was slower and more difficult The muscles showed tremblings and the hind legs were weak Feeding dried prostate caused marked improvement —T C B

QUINCKES' EDEMA in the Danish medical literature Faber (K),
Ugesk f Læger (Copenhagen), 1919, 81, 448-449

The author notes that Christoffersen's case (Endocrinol, 3, 385) was not the first in the Danish literature. Cases have been reported by Lange, Dreyer, Strandgaard and Rasch —K H K

Function of the SPLEEN (Beitrage zur Physiologie der Drusen
LIII Die Funktion der Milz, insbesondere bei normalen und
erhohtem Sauerstoffbedarf) Bernet (E), Biochem Ztschr
(Berl), 1922, 128, 250-267

Working with rabbits the author found that no increase in ammonia excretion occurs during increased oxygen want. When the spleen is removed a change in the ammonia excretion may take place, but this is not influenced by increased oxygen demand. Splenectomized rabbits excrete more nitrogen in the urine than do normal rabbits. This signifies an increased protein decomposition when the spleen is removed and leads to the idea that this organ has a regulatory influence on metabolism in the sense of a sparing action. When the oxygen demand is increased in splenectomized rabbits the nitrogen excretion is also increased. Pneumothorax was the means employed to produce an increased oxygen demand —F S H

(SPLEEN) Recent investigations on internal secretions (Osservazioni
in toro ad alcune recenti ricerche nel campo delle secrezioni
interne) Patta (A), Boll d Soc med-chir di Pavia (Milano),
1919 (No 4), Abst, Pathologica (Genova), 1922, 13, 60

The intravenous injection of venous blood from the normally appearing spleens of normal animals led to diminished blood pressure and pulse rate, followed after a few minutes by normal or even elevated pressure. Even a greater amount of blood from a small, hard spleen with thickened capsule did not cause any modification either of pressure or of the pulse —G V

Influence of local application of TESTICLE substance on cicatrization (Il processo di cicatrizzazione delle piaghe sotto l'influsso di applicazioni del parenchima testicolare) Ajevoli (E), Riforma med (Napoli), 1921, 37, 947-949

A summary of the findings of Voronoff and Bostwick in their experiments of pancreas, thyroid, adrenal and testis as topical application on sores. The author takes occasion to recall his experience, published in the Riforma med, 1890 —G V

Report of a case of cyst of the TESTICLE in a dog Barach (A L),
Proc N York Path Soc (N Y), 1919, 19, 38-50

This is a report of a careful study of a case of cyst of the testicle which followed trauma in a dog, with a discussion of the patho-

genesis of non-retention cysts The article has a special interest for pathologists, but no immediate endocrine interest —J P S

Pathological changes in the TESTES in constitutional diseases, particularly marasmus (Pathologisch-anatomische Veränderungen der Keimdrüsen bei Konstitutionskrankheiten, im besonderen bei der Padatrophie) Jaffe (R), Frankfurt Ztschr f Path (Wiesb), 1921, 26, 250-267

This study was made in the Pathological Institute, University of Frankfurt The author points out that autopsy findings in marasmus are generally negative From a study of the testes in normal children and in marasmus he comes to the conclusion that the most certain criterion for the anatomical diagnosis in children's testes is the number of interstitial cells and their fat content In the testes of normal children one finds very little connective tissue, the interstitial cells are few and either contain no fat or at most only traces of fat In chronic infectious diseases there may be a secondary atrophy In such cases one finds the stroma between the seminiferous tubules increased and edematous, the interstitial cells show no change from normal In children with a clinical diagnosis of constitutional inferiority, one notes a definite increase in the connective tissue stroma and in the interstitial cells, both in number and in lipid content These are the changes usually found in children with marasmus The increase of interstitial cells and their fat content is not looked upon as a cause of the condition but rather as the manifestation of constitutional inferiority —D M

(TESTES) Experimental retardation of masculinization (Ralentissement expérimental de la masculinisation) Lipschutz (A), Wagner (C) & Bormann (F), Compt rend Soc de biol (Par), 1922, 86, 238-240

Horizontal incisions were made into the testicles of a rabbit two months ago On the right side the incision was made into the epididymis, on the left side, not The control rabbit born the same day attained puberty at the age of four months and a half, the other, not until about seven and a half months The histology of the testicles is given —T C B

(TESTES) Vasectomy in a dog as a regeneration experiment Sand (K), Ugesk f Læger (Copenhagen), 1921, 83, 1509-1516

The case is described of a dog, aged 12 years, very senile, emaciated and miserable For a time after vasectomy on the left side and resection of epididymis on the right, the dog remained very miserable, but after 3-4 weeks it improved markedly The movements became more rapid, the hair grew better, the appetite increased and the dog regained its earlier vigor —K H K.

Urethral malformations accompanied by TESTICULAR anomalies
(Sulla concomitanza di alcune malformazioni uretrali con anomalie testicolari) Torraca (L) Riforma med (Napoli), 1921, 37, 1093-1095

Not of endocrine interest —G V

Sudden death of two children in the same family THYMIC death in hereditary syphilis (Morte improvvisa di due bambini nella stessa famiglia Sulle morti timiche in ereditarie) Battino (C), Pediatria (Napoli), 1922, 30, 248-256

The author reports a case of a girl, 6 years old, whose brother at the age of 4 had died suddenly. There was psychasthenia on her father's side and tuberculosis on her mother's. No hereditary syphilis showed in the children. Two brothers were living and apparently well. All of them were well nourished but pale. The girl, apparently well, after a hearty meal at home, ate again with a sound appetite a few hours after. Suddenly, without any symptom, she fell dead. Autopsy disclosed nothing abnormal in the abdomen except congestion and distension of the stomach and intestines. Upon opening the thorax a thymus was found of the length and width of the sternum, but without cysts, gummata or hemorrhages, there were no signs of compression. The lymphatic system was rather well developed. Since there was no cyanosis or spasm of the glottis, the author believes that, if the death be ascribed to nervous inhibition, the sympathetic fibres to the thymus might have been involved rather than the sensory nerves of the trachea. Anaphylactic shock due to hypersecretion of the thymus seems more likely to have caused the death. A positive Wassermann test was later obtained in both parents —G V

Anatomical and pathological study of the THYMUS in infancy (Contributo allo studio anatomico e pathologico del timo nella prima età) Canelli (A F), Pediatria (Napoli), 1921, 30, 58-64

The author has studied the formation of "Gitterfasern" in normal and in pathological cases. In patients with normal thymus the following conclusions were reached. In the first five months of intrauterine life only a few of these fibres can be found either in the cortex or in the medulla, and these mostly around the vessels. From birth to 3 years of age the "Gitterfasern" are not much more numerous, yet the perilobar reticulum is more evident and some fibrillae from the reticulum and from the perivascular sheets proceed toward the parenchyma. From 4 to 15 years of age they become numerous,—more so at the periphery than in the central part in both the cortex and medulla, but they are never seen either around or in the Hassel's corpuscles. After the 16th year of age they become quite predominant, especially in the cortical part, but some are also found around the Hassel's corpuscles, especially if calcified.

In adipose degeneration when the distinction between cortex and medulla almost disappears they are quite numerous in the fatty tissue. They are lacking in the cords of epithelial cells, except around vessels or in the connective formations. From this the author infers that their lack in the epithelioid tracts evidences the epithelial nature of these tracts. In patients with pathological thymi, without distinction of age, the "Gitterfasern" are greatly developed —G V

(THYMUS) Caseated thymoma of the mediastinum Cleland (J B) & Beare (F H), Med J Australia (Sydney), 1922, 1, 182

A case report. The tumor was 6.2x5x3.7 cm, it reached almost to the base of the neck and was firmly adherent to the aorta. It was largely necrotic but showed areas of typical thymus tissue. Aside from the tumor no gross abnormality was found —R G H

THYMIC and pseudo-thymic stridor (Stridore timico e stridori pseudotimici) Cozzolino (O), Pediatria (Napoli), 1921, 20, 729-743

The article is a discussion on the various conditions, besides enlarged thymus, which may provoke stridor. A number of thymic cases greatly improved by radium therapy is reported —G V

(THYMUS) A case of Erb-Goldflam's disease (Su di un caso di morbo di Erb-Goldflam) D'Amato (L), Riforma med (Napoli), 1921, 37, 1204

In connection with a case report D'Amato mentions that he has found that the removal of the thymus gland of myasthenics may result in damage to the function and the structure of the muscles —G V

A case of THYMOMA Ewing (J), Proc N York Path Soc (N Y), 1919, 19, 156-160

Of no immediate endocrine interest —J P S

A case of THYMOMA Klengenstein (P), Proc N York Path Soc (N Y), 1919, 19, 151-156

Of no immediate endocrine interest —J P S

A tumor of the THYMUS gland Rohdenburg (G L L), Proc N York Path Soc (N Y), 1920, 20, 97-99

Of no immediate endocrine interest —J P S

Chronic inflammation of the THYMUS Schmorl, Gesell f Naturf u Heilk (Dresden), 1919, Abst, Pathologica (Genova), 1922, 13, 34

The author reports a case of chronic thymitis in an infant 9 months old who did not show any symptom of it while living. There was no rickets. The patient had undergone tracheotomy nine days before and the author concludes that even in so short a time thymic lesions could have formed.—G V

THYMUS tumors (I tumori epiteliali del timo, di un caso de adenoma del reticolo timico) Vanzetti (F), Arch per le sc med (Torino), 1917, 40, 264-307

References verified from Index Medicus

Lymph follicles with germinal centers in the THYMUS medulla (Ueber Lymphfollikel mit Keimzentren im Thymusmark) Wegelin (C), Centralbl f allg Path u path Anat (Jena), 1918, 29, 441-447

The author refers to reports in the literature in which definite lymphoid tissue was reported in the medulla of the thymus, especially in Graves' disease, and reports the case of an eleven year old girl, operated on in the Surgical Clinic at Bern, in which a large goiter together with the cervical portion of the hyperplastic thymus was removed. There were many clinical manifestations of status thymicolymphaticus. He believes that the presence of germinal centers in the thymus medulla is very rare, but that they may actually occur in both the hyperplastic thymus of Graves' disease and status thymicolymphaticus. He then discusses whether the lymphoid elements of the thymus are entirely epithelial or of mixed epithelial and lymphatic origin. His studies support the views held by Hammar, Maximow and Hart that the small thymic cell originates from migrated blood and lymphoid elements.—D M

Auto-transplantation of the THYMUS in the spleen of rabbits (Ueber autoplastische Transplantation der Thymus in die Milz bei Kaninchen) Yamanoi (S), Frankfurt Ztschr f Path (Wiesb), 1921, 26, 356-381

The author reviews some of the literature on both homio- and auto-transplantation of the thymus and points out the failure of all homiographs. The results reported were obtained on thirty rabbits, mostly adults, as young rabbits did not withstand the operative procedures well. Various sites have been used for transplanting the thymus, but the author selected the spleen, introducing the thymic tissue immediately after its removal by means of a trocar and stylet. He obtained the thymic tissue by dividing the sternocleidomastoid muscles, pulling up the thymus and amputating part of it. The effect, therefore, of a thymic deficiency on the life history of the graft was not studied. He studied the transplants microscopically from 1 day to 163 days after implantation. In only three animals did the transplants survive longer than 100 days. He found the usual de-

struction of the transplanted thymic tissue during the first few days. On or after the fourteenth day definite regeneration of thymic cells was found, this included Hassall's corpuscles and the true small cortical lymphocytes. He was not able to study the fate of the transplanted thymic eosinophil in this material, but has undertaken another series of experiments to investigate this point. The theories of origin of the small cortical thymic cells are discussed, i. e., whether they arise from epithelial elements, as Stohr and others have claimed, or from the blood and lymphoid tissue as Hammar, Maximow and others hold. He supports the view that these small thymic cells are derived from the epithelial thymic elements. Abstracter's Note. It is doubtful whether the spleen offers the best site for the study of tissue transplants from bone marrow, lymph glands or thymus.—D M

Treatment of emesis with **THYROIDINE** Albeck (V), Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 44-46

The author has formerly found that most cases of emesis are complicated with very small thyroid glands. He has therefore tried to treat a number of cases of emesis with thyroidine. In cases of slight severity results were not marked enough to consider, but 20 very severe cases which were treated with thyroidine, 15 cgm, every day, showed a very marked improvement. Some were completely cured.—K H K

The relation between emesis and the size of the **THYROID**, and demonstration of a strange modification of the thyroid in sows with young. Albeck (V), Ugeskr f Læger (Copenhagen), 1919, 1047-1054, 1083-1087

The author has observed that there is a constant relation between the cases of emesis and the size and consistency of the thyroid, women with a large and soft thyroid never have emesis during pregnancy, while women with a small, hard thyroid always have emesis. In 23 cows with young the author found the weight of the thyroid to be 4.57 gm per 100 kg body weight, in cows without young 4.35 gm. In 34 sows with young the weight of the thyroid was 14.58 gm per 100 kg, in 163 sows without young, 15.65 gm. In 3 sows with eclampsia the weight was 12.31 gm, but the individual variations were too great to permit conclusions. Histological examinations showed that the thyroids in sows with young were modified from the 3d to the 4th week. In the middle of pregnancy the organ showed complete adenomatous structure with very many and very small follicles, with cubical or cylindrical epithellum, often in several layers. At the end of pregnancy these modifications disappeared. The modifications are different from those in rabbits and guinea-pigs described by Engelhorn, but they are like the changes in cats described by Borzystowsky.—K H K

(THYROID) The cause of cretinism (*Sulla causa del cretinismo*) Allara (V), *Attualità med* (Milano), 1916, 5, 432

Reference verified from Index Medicus

(THYROID) Etiology of endemic goiter and cretinism (*Nuove vedute sull'etiologia del gozzo endemico e del cretinismo*) Arcangeli (U), *Studium* (Napoli), 1916, 9, 65-70

See Endocrin, 1, 103

(THYROID) Diagnosis and therapy of Graves' disease Bang (S), *Hosp-Tid* (Copenhagen), 1921, 64, Danish med Soc reports, 20-26

It is very difficult to compare statistics on Graves' disease, especially since some authors believe that exophthalmos is always present, while others find it in only 50-70% The author warns against too inclusive use of the term "Graves' disease" Perhaps the method of Krogh will help in a more exact diagnosis The author recommends beginning with hygienic-dietetic treatment, to be followed by x-ray therapy In the cases that are not cured by this treatment, operation is recommended —K H K

(THYROID) Etiology of goiter (*Per il quesito etiologico del gozzo*) Bertarelli (E), Morgagni (Milano), 1916, 58, 693-696, *Riv d'ig e san pubb*, 1916, 27, 481-485

Reference verified from Index Medicus

(THYROID) Infantile mongolianism (*Mongolisme infantile*) de Biehler (M), *Arch de méd d enf* (Par), 1922, 25, 81-89

A general discussion of the clinical symptomatology of mongolian idiocy in infancy Four cases are reported in brief In two a slight improvement was noted following the administration of thyroid extract in doses of 0.05 gm thrice daily —C H G

(THYROID) Common types of goiter Bram (I), *Penn M J* (Harrisburg), 1922, 25, 336-345

Clear differential pictures are presented of the types of non-toxic and toxic goiter Special emphasis is placed on the proper recognition and differentiation of toxic adenoma, as distinguished from hyperplastic goiter (exophthalmic goiter, Graves' disease) There is a concise tabulation of the principal signs and symptoms, history and course of these two common thyroid disorders The various diagnostic tests for toxic goiter are commented upon The differential blood count, Harrower's thyroid extract test, complement fixation test, hyperglycemia test, mydriasis test, pituitary test and adrenalin hypersensitiveness test are not considered very valuable or reliable The determination of the basal metabolic rate and

the author's quinine test are helpful and trustworthy The prompt curative result of surgical procedures in toxic adenoma is admitted, but surgery is regarded as unwise, if not contraindicated, in the exophthalmic type —H L

(THYROID) Congenital megacolon and myxedema (Megacolon congenito e mixedema) Cattaneo, *Pediatrica* (Napoli), 1921, 20, 661

The author reports a case of congenital megacolon involving the ampulla and the descending colon A condition of myxedema was found and thyroid medication prescribed The myxedematous condition not only disappeared, but the constipation was cured, and a second x-ray picture taken after the treatment showed the descending colon normal In cases of congenital megacolon the author insists on the necessity of looking for an endocrine dysfunction

—G V

(THYROID) Are there reliable criteria of operability in exophthalmic goiter? Cheever (D), *Arch Surg* (Chicago), 1921, 2, 21-36

Cheever attempts a formulation of exact criteria of the ability of the thyrotoxic patient to withstand operation, stressing as contraindications acute exacerbations, muscular weakness, continued marked weight loss, serious organic visceral disease, enlarged thymus (present in 75% of exophthalmic cases) unless irradiation is effective in decreasing thymic activity, a basal rate of plus 30 or more, severe reactions after minor surgical procedures, such as injections into the gland, cauterizations or ligations He believes the evidence supporting the contention of Means and Aub (*Arch Int Med*, Chicago, 1919, 24, 645) that 'vagotonic' syndromes offer greater vulnerability than those of the sympatheticotonic type, to be inconclusive Unfortunately many factors concerned in the toxemia are not susceptible of accurate measurement, moreover, in hyperthyroidism, operations will always be attended by a peculiar factor of danger, not present in other operations which are technically similar —C R

(THYROID) Handling of the toxic goiter under ether-oil colonic anesthesia Dickinson (G K), *Am J Surg* (N Y), 1922, 36, 40-42

Because of the emotional state in toxic goiter due to thyroid and adrenal activity, Dickinson endorses Crile's technique for "stealing the goiter," but substitutes ether-oil colonic anesthesia for nitrous oxide His own results have been excellent, but he believes that the method should be more widely used and reported upon before it can be regarded as a proven procedure —C R

THYROIDECTOMY and PARATHYROIDECTOMY with relation to the development of immune substances Ecker (E E) & Goldblatt (H), J Exper M (Balt), 1921, 34, 275-294

The authors attempted to determine the relation of thyroidectomy and parathyroidectomy to the development of immune bodies. They compared power of recovered thyroidectomized and thyroparathyroidectomized animals to develop anti-sheep hemolysin with that of normal animals. After thyroidectomy and partial parathyroidectomy in rabbits the average and maximum hemolytic titers of the sera were equal to, or higher than, those in normal animals injected with sheep blood in the same way. After complete thyro-parathyroidectomy a small proportion of the animals lived, even after developing very severe tetany. In these animals the anti-sheep hemolysin developed by the same technique was of a uniformly low titer,—on an average, one-fifth that of the controls—I M

(THYROID) Cachexia strumipriva with marked ascites as dominant symptom Faber (K), Ugesk f Læger (Copenhagen), 1919, 81, 1403-1408

From the age of 15 years a girl showed enlargement of the thyroid, at the age of 23 years strumectomy was performed. The goiter consisted predominately of colloid tumour and cysts. After the operation she was well for 2 years, then severe ascites set in with headache and loss of hair. The ascites receded after punctures. Laparotomy was performed to make possible a Talmas operation, but the liver and all the abdominal organs were found normal. After each paracentesis ascites recurred. In one year 11 punctures and two laparatomies were made. After treatment with thyroïdine there appeared a very marked diminishing of the ascites. Upon discontinuation of the thyroïdine ascites recurred, but disappeared completely when the thyroid treatment was renewed. Also the myxoedematous symptoms disappeared. The author believes that the ascites is definitely to be ascribed to hypothyroidism, and as analogous with the thyroprivic edemata described by Eppinger. The ascitic manifestation appears to be unique, so far as the literature disclosed. Sodium chloride metabolism was found normal by the Strauss test—K H K

Abdominal and THYROID galvanization as a treatment of hyperthyroidism (*La galvanisation abdomino-thyroïdienne dans le traitement des syndromes d'hyperthyroïdie*) Foubert (F), These de Paris, 1921

Galvanization with electrodes on the abdomen and thyroid has a good effect in hyperthyroidism and in Graves' disease. The treatment has no contraindications and is absolutely without danger. The thyroid can stand a much stronger current without disagreeable symptoms than other parts of the body. Combination with

other treatment is possible and may even be advisable (for instance, x-rays) The effects on the tachycardia, the goiter, the exophthalmus and diarrhea are especially remarkable Operation is indicated only in cases where even this treatment fails, which is very rare —J K

Urticaria and HYPOTHYROIDISM (*Orticaria ed ipotiroidia*)
Fubini (E), *Pathologica* (Genova), 1922, 14, 27-30

Report of a case of urticaria lasting nine years in a woman 30 years old She first menstruated at 18 She shows a complete syndrome of hypothyroidism, enophthalmus, small thyroid, tendency to adiposity, scarce, irregular menstruation, frigidity, dry skin and hair, characteristic eyebrow, brittle nails with white spots, easily acquired colds, several spells of bronchial asthma and a great sensibility to cold and hypothermia Except for these symptoms the general examination was negative She underwent years of treatments of all kinds, but found no relief except when treated with pluriglandular therapy, and this was but slight The patient was then put on general diet and given injections of "endotiroidina." In a few days a remarkable improvement began, leading to a practical recovery The author believes urticaria due to anaphylaxis, which, according to his opinion, may be induced by external protein as well as by protein formed in the organism He is inclined to believe, also, that owing to the dysfunction of the thyroid abnormal proteins may be liberated from the thyroid giving origin to anaphylactic trouble, with analogous mechanism to hetero-proteins —G V

The iodine content of the THYROID in the Japanese adult Fukushima (T), *Nikan Naikagakkwai Zasshi*, 9, No 5, Abst, Jap Med World (Tokyo), 1922, 2, 45

The author determined the iodine content of the thyroids of subjects free from any complication with thyroid disorders He used the Bowman-Anten's color reaction test for iodine He found that the total weight of the Japanese thyroid was one-third that in Europeans It was equally distributed in the lobes, being 0.81 mg per gram of fresh glands The comparative iodine content appeared to be higher in the Japanese, possibly due to difference in the food There was no distinction in iodine content of thyroid in patients with different diseases or diseases extending over varying periods Generally considered, the iodine content of the thyroid varied more with the administration of iodine preparations, especially those given internally —R G B

(THYROID) Experimental goiter produced by fluorine (*Goitre experimental par le fluor*) Goldemberg (L), *Semana méd* (Buenos Aires), 1921, 28, 628

The addition of 2-3 mg sodium fluoride to the food of young white rats during a period of six to eight months produced chronic

intoxication with retarded growth, etc The thyroid increased in size, its parenchyma became compact, with considerable cellular hyperplasia The author considers that this enlargement amounts to experimental goiter—B A H

The influence of THYROID products on the production of myocardial necrosis Goodpasture (E W), J Exper M (Balt), 1921, 34, 407-423

Finding acute necrosis of the cardiac muscle at autopsy in patients dying of myocardial exhaustion from hyperthyroidism, the author has studied the effect of desiccated thyroid and thyroxin in large doses to determine whether such hearts are more readily injured by toxic agents, such as chloroform, than normal hearts Healthy young rabbits under standard conditions were given, in one series, 1 mg of desiccated thyroid per day by mouth and, in another, 1 mg of crystalline thyroxin intravenously every second or third day over a period of two to three weeks A similarly treated series of animals was given, in addition, after the thyroid effects were fully developed, one hour of light chloroform anaesthesia The clinical effects of the thyroid were marked in all cases, the pulse rate increasing about 50% and the weight decreasing markedly When the animals were sacrificed at the end of two or three weeks, the series receiving thyroid products only showed no gross lesions and, microscopically, relatively insignificant changes only, in the form of perivascular fibrosis The injury appeared to have been produced by the first doses given, with a subsequent attempt at repair The second series, in which the animals received one hour of light chloroform anaesthesia 24 hours before being sacrificed, showed very definite focal necroses of the myocardium, both macroscopically and microscopically Control animals showed no such changes with chloroform alone and the author concludes that a heart stimulated to abnormal activity by thyroid products is more susceptible to injury from poisons of acute infections, chloroform, etc, than is a normally acting heart—I M

Hypoplasia of the THYROID in an infant (Hypoplastische Schilddrüse von einem Säugling) Graupner, Deutsche med Wchnschr (Berl), 1922, 48, 144

Demonstration of the hypoplastic thyroid of an infant who had enormously developed muscles—J K

Tuberculosis with THYROID manifestations (Tuberculosis a manifestazioni tiroidee—tiro-tuberculosis) Janowski, Riforma med (Napoli), 1921, 37, 344-345

Report of an article published by Janowski in the Ann de Med, 1921—G V

Results on an enlarged THYROID gland nine years after obstructing the veins Guthrie (C C), *Am J Physiol (Balt)*, 1922, 50, 447

Following a short period of enlargement after ligation of all the major veins to the left lobe, it greatly diminished in size. The bitch was killed in a fight nine years after operation. The left lobe was subnormal in size, but showed normal appearing areas of thyroid alveoli and colloid. More fibrous tissue was present than normally.

—T C B

(THYROID) Systematic goiter therapy and prophylaxis (Ueber systematische Kropf-Therapie und Prophylaxe) Hunziker (H) & Wyss (M v), *Schweiz Med Wchnschr*, 1922, 52, 49-54

This report is based on some additional observations by Hunziker and Wyss on a group of 775 goitrous school children. Extensive tables, which indicate the relation of goiter incidence, size and decrease (under treatment) in relation to sex, height and weight, nodular formation, age, effects of vicarious treatment, etc., are given. For prophylaxis, potassium iodide is used. Preference is given to this salt rather than to organic compounds. Standardized doses of KI are not recommended. Better results are believed to have been obtained from doses adjusted to age, physical condition, size of goiter, geographic situation of affected groups, etc. The doses as used, approximated one mgm of KI per week throughout the year. This procedure was found both to reduce goiters already existing and to prevent goiter formation in the normal individual. These authors conclude that both goiter prophylaxis and goiter therapy on a wide basis may be profitably carried out in schools.—C P McC

The influence of THYROID preparations on the blood picture and especially on eosinophilic cells Kamikozawa (Y), Igaku Chuwa Zasshi (Tokyo), No 349, *Abst, Jap Med World (Tokyo)*, 1921, 1, 18

After thyroid extract was administered in 6 cases of bronchial asthma a decrease in the number of eosinophiles followed within 7-10 days and persisted over varying periods. There was a corresponding improvement in the pulmonary condition. In a few cases there was a slight increase in eosinophiles at the beginning, giving place later to decrease. In three cases of ankylostomiasis, a lowering in the number of white blood cells with a relative increase in polynuclear cells resulted. There was an absolute increase in eosinophiles. Similar conditions were seen in vagal eosinophilia. In normal patients thyroid caused no change in the eosinophilic count. Drugs increasing the tension of the sympathetic nerves cause an increase in polymorphonuclear neutrophilic and a decrease in eosinophilic cells, while those increasing the tension of the vagi produce an increase in mononuclear and eosinophilic cells.—R G B

(THYROID) Technique of complement fixation in Basedow's disease
 Koopman (J), Proc N York Path Soc (N Y), 1921, **21**, 56-57

The blood of some patients with symptoms of Basedow's disease binds complement in the presence of an antigen made from normal glands To prepare the antigen, the glands of dogs are obtained under aseptic precautions as soon as possible after death All extraneous tissue is removed and the gland is minced finely with sterile scissors The mass of thyroid is weighed carefully and is then ground in a mortar with washed, sterilized sand and an amount of sodium chloride equal to one-tenth gram for each gram of gland used A few drops of 2 per cent tricrosol is added for each 10 grams of thyroid, and the mixture is bottled and kept in the icebox For use, 10 cc of distilled water is used for each gram of gland in the suspension of sand and ground thyroid The sand and solid matter are removed by centrifugation A mixture of thyroids from several dogs is recommended This antigen, which necessarily contains much extraneous matter, deteriorates slowly and after about three weeks it is necessary to secure a new supply The test is set up in the form of a titration, using a constant amount of the patient's serum, which is not more than one-fourth of the quantity which is anti-complementary The antigen is used in varied amounts, beginning with an excess and ending with the least amount that can be expected to give fixation of complement At the same time the anti-complementary titer of the antigen is determined by setting up a series of control tubes containing the same quantities of antigen as used in the test The result is indicated by the difference between the quantity of antigen that is anti-complementary of itself and the quantity that binds complement in the presence of serum A negative serum with antigen will often bind less complement than the antigen alone A serum is considered positive when it binds complement in the presence of one-half or less than one-half of the anti-complementary dose of antigen, and the smaller the amount of antigen necessary for complete fixation the stronger the reaction Fixation is carried out for from four to six hours in the icebox

—J P S

Three cases of vagotonia, complicated by irregular pulsation, with special reference to the influence of THYROID Kozawai (Y), Chugai Iji Shinpo (Tokyo), No 995, Jap Med World (Tokyo), 1922, **2**, 47

The author administered thyroid material to certain patients having irregular pulsation occurring with vagotonia The first had Stokes-Adams' disease and typical vagotonia The second had bronchial asthma and auriculo-ventricular pulsation The third had exophthalmos and, after x-ray treatment, showed signs of vagotonia In these three cases, thyroid administration was followed by remarkable results, for the symptoms either disappeared or were greatly

ameliorated In the last case, eosinophilia was completely suppressed and the heart action improved Thyroid preparation augments sympathetic activity and thus mitigates vagotonia ("Vagotonia" is "strain of the vagus" in the abstract from which this is taken—Ed)—R G B

(**THYROID**) Gastric secretion in Graves' disease Kramer-Petersen, Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 46-48

In 12 cases of Graves' disease the author found severe diarrhea in 7 and achylia or hypochylia in 10 There was no disturbance of the motor function of the stomach—K H K

Determination of the respiratory metabolism, especially in patients suffering from **THYROID** diseases Krogh (M), Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 3-7

Diseases of the thyroid manifest themselves in the total energy changes Respiratory metabolism serves as an index of these In myxedema the metabolism may be diminished to 60%, in Graves' disease, increased 100% Metabolism examinations are therefore necessary in thyroid diseases, especially in cases in which the diagnosis is uncertain or before thyroid operations The examinations employed in the Mayo Clinic are somewhat difficult for the ordinary practitioner to employ, the gas analysis is difficult The author therefore has made her examinations with a respiratory apparatus constructed by August Krogh The patient respire in a registering spirometer in the bottom of which there is a box containing 8 kg sodium hydrate and calcium hydrate The inspired air passes under the box, the expired, over it Before the examination the reservoir of the spirometer is filled with oxygen The reservoir will sink during the whole experiment, while the patient absorbs the oxygen, and the carbonic acid is absorbed by the hydrates The degree of filling of the spirometer and the respirations are registered on a rotating cylinder, moving 2cm per minute If the curve of respiration is irregular the result is without significance The result can otherwise be calculated from the curve—K H K

Glande **THYROIDE** et anaphylaxie Lauzenberg (A) & Képinow (L), Compt rend Soc de biol (Par), 1922, 86, 204-206

A study of anaphylactic shock in animals deprived of the thyroid Guinea pigs were thyroidectomized and kept for a week before beginning the experiment Controls were chosen of the same weight The sensitizing dose was subcutaneous, the anaphylactic, by the carotid The lethal dose was 1 cc of a tenth dilution serum Eight thyroidectomized animals were sensitized on the day of the operation Twenty days later they received a lethal dose of serum All the controls died Six of the thyroidectomized animals are still

living Three had a slight dyspnoea, but none of them had anaphylaxis Of the two that died, one was autopsied and a bit of thyroid was found, which may account for death When only half of the thyroid was removed, all died, both experimental and control, with the classic symptoms of shock In another series, the animals were sensitized and twenty days later the thyroids were removed Twenty-seven days after sensitization the anaphylactic injection was given Both groups died To sum up, there was no anaphylaxis when thyroidectomy was done before sensitization Removal of the thyroids after sensitization does not prevent shock A later communication is promised —T C B

(**THYROID**) Eye symptoms in Graves' disease Lindgren (E), Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 36-44

A discussion of the frequency of the different eye symptoms in Graves' disease —K H K

(**THYROID**) A case of myxoedema (Un caso di mixedema) Luzatto (A), Riforma med (Napoli), 1921, 37, 787

A baby girl one year old showed from the 8th month of life myxoedematous appearance, prognathism, macroglossia, prominent abdomen and cyanosis of the limbs Thyroid medication gave satisfactory results (dose 0.15 gm daily) —G V

(**THYROID**) Are iodides foods? McClendon (J F), Science (N Y), 1922, n s 55, 358-361

A discussion of the distribution of iodine from sea water spray and its relation to goiter prevention The use of an impure salt from sea water is suggested in order to furnish iodine —F A H

(**THYROID**) Two cases of myxoedema in children Margulis (B I), Prakt Vrach (Petrogr), 1916, 15, 170-183

Reference verified from Index Medicus

Extensive bone formation in the **THYROID** Meyer (H W), Proc N York Path Soc (N Y), 1919, 19, 70

A very brief presentation of an adenomatous thyroid "with not only deposition of lime salts within the stroma, but also extensive formation of true bone" —J P S

(**THYROID**) Etiology of chorea (Sulla etio-patogenesi della corea del Sydenham) Millo (G), Pediatria (Napoli), 1921, 29, 360-363

Silvestri is quoted to the effect that hyperthyroidism may be a cause of chorea, since it developed in two children being treated with thyroid preparation for adenoids and ceased when the thyroid was discontinued Simonini relates the disease to parathyroid insuff-

ficiency since, in a woman who died after repeated attacks of chorea, he found hypoplasia of these glands —G V

(THYROID) Endemic goiter, histology and therapy (Gozzo endemico, istologia e terapia) Muggia (G), Riforma med (Napoli), 1921, 37, 738

The author calls this kind of goiter "mountain thyroid" and he claims that where the goiter is endemic there is no such a thing as a healthy thyroid. He found, besides the well known hypertrophy, small follicles deprived of colloid with cubical epithelium, showing more or less fatty degeneration. A gradual connective hyperplasia follows and finally, cystic degeneration and calcification. The connective hyperplasia is precocious and the volume of the gland has no connection with the severity of the lesion. Muggia emphatically denies infection as a cause of goiter and refers it to geologic and meteorologic conditions (pressure, rarefaction of air and deficient oxygenation). Opotherapy proves very efficacious and has to be continued until the size of the gland approaches normal. Little improvement in the intelligence has been seen —G V

(THYROID) Cases of Graves' disease Nordentoft (S), Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 31-36

The author has treated 150 cases of Graves' disease with x-rays. No mortality resulted and they were for the most part improved or cured. He describes more in detail two severe cases, those of a mother and a daughter, who were cured. He considers the dangers from x-ray treatment very slight. He maintains the desirability of considering a thymic factor in Graves' disease, which he has mentioned in former articles —K H K

(THYROID) The toxic goitre Ohara (H), Nisshin Igaku, 10, No 10, abst, Jap Med World (Tokyo), 1921, 1, 23

Leucocytes markedly increased the blood viscosity (3.7 to 6.2, mean 5.12) possibly due to increase of leucocytes. Thyroid secretion in Basedow's disease caused an increase of adrenalin and sugar content of the blood. Coagulability was decreased, possibly due to autolysis of fibrin due to thyroid secretion. The resistance of the erythrocytes was markedly increased but fell to normal following extirpation of the gland. Alimentary adrenal glycosuria may be applied to determine the severity of the disease. The author concludes that extirpation of the thyroid is an ideal treatment in bringing the changed blood to normal —R G B

(THYROID) Toxic goiter Ohara (H), Nisshin Igaku, 11, No 1, abst, Jap Med World (Tokyo), 1922, 2, 55

The author dealt with the influence of toxic goiter on the circulatory organs. The heart is especially affected —R G B

(THYROID) Anemia and goiter (II Communication) Ohara (H), Nisshin Igaku, 10, No 12, abst, Jap Med World (Tokyo), 1922, 2, 22

There may be anemic manifestation in simple and exophthalmic goiter but true anemia is not necessarily present and so when present is not necessarily due to the goiter —R G B

(THYROID PARATHYROIDS) Studies on the amino-acid nitrogen content of the blood Okada (S) & Hayashi (T), J Biol Chem (Balt), 1922, 51, 121-133

These studies of the amino-acid nitrogen content of the blood of dogs and rabbits show that the removal of the thyroid gland or of the parathyroids, from which latter procedure tetany is developed, causes an appreciable change in this fraction of the blood nitrogen. Five cases of Graves' disease were examined and the amino-acid content of the blood was normal in all. The thorough removal of the pancreas causes a transient increase of amino-acids in the blood. When a part of the pancreas is left under the skin in connection with the circulation of the blood the amino-acid nitrogen remains normal —F S H

The glycogen content of the liver and muscles in THYROIDECTOMIZED animals (Sur la teneur en glycogène du foie et des muscles chez des animaux éthyroïdés) Parhon (Marie), J de physiol et de path gén (Par), 1921, 19, 198-201

Mme Parhon reviews briefly the literature dealing with the blood sugar, glycogen content of liver and muscles, and sugar tolerance in thyroidectomized rabbits, dogs, sheep and guinea pigs. Observations are reported on the glycogen content of the liver and muscles of five normal guinea pigs, five thyroidectomized guinea pigs, two normal sheep and three thyroidectomized sheep. The guinea pigs were adults while the sheep were about six weeks old. The thyroidectomized guinea pigs were allowed to live six or seven months and the sheep fourteen to fifteen months before sacrificing. The glycogen content of the liver of the thyroidectomized animals was slightly less than that of the controls. This could not be explained on the basis of increased consumption. The author therefore believes that in thyroidectomized animals the sugar absorption from the alimentary tract is slower and less complete than normal, and that this also is the most probable explanation of the so-called increased alimentary tolerance for sugar in thyroidectomized animals. (The diet does not appear to have been controlled and the very long period the animals were allowed to live after thyroidectomy gives sufficient time for compensation which we know occurs with great frequency in animals) —D M

(**THYROID**) Exophthalmic goiter with marked vasomotor symptoms
(Forma frusta di morbo di Flaiani-Bascdow con sintomi spiccati
di natura vasomotoria) Pennisi (A), Riv osp (Roma), 1917,
6, 712

Reference verified from Index Medicus

The treatment of carcinoma of the **THYROID** by the Roentgen rays
and radium Pfahler (G E), Am J Roentgenol (Detroit), 1922,
9, 20-25

Dr Pfahler finds no record of the treatment of carcinoma of the thyroid by radiation, but suspects that other cases have been reported under more general terms His experiences have extended over a period of eleven years and the results have been generally most gratifying, for in nearly all instances the treatment was used in an otherwise hopeless group and yet the results have been in some cases brilliant He places on record ten cases Case 1 was treated in 1910 and had been previously operated upon three times for carcinoma of the thyroid and recurrences The treatment given in 1910 was for a recurrence consisting of an indurated mass in the region of the wound, immediately above the clavicle on the right side and another indurated moveable tumor mass, 2.5 cm in diameter, located below the mastoid on the right side Under treatment the patient apparently regained health for about a year and there was no local recurrence at any time, but about eighteen months after beginning treatment she developed signs of metastasis in the first cervical vertebra, from which she died two years and one month after beginning treatment Case 2 involved a large tumor of the right lobe of the thyroid extending down into the upper mediastinum The tumor was radiated in 1911 The patient was well when last heard from in 1918 Case 3 was treated in 1913 after operation by Dr John B Deaver in which he was unable to remove all of the diseased tissue The patient was still well September 19, 1921 Case 4 had been operated upon twice, first under the diagnosis of branchial cyst involving the right side of the neck and second for a recurrence of the tumor involving the right lobe of the thyroid This was found by microscopical examination to be adeno-sarcoma A re-study of the original tumor showed it to be malignant At the time of beginning x-ray treatment radioscopy of the chest showed an abnormal shadow about the roots of the right lung and extending upward along the right mediastinum The patient was treated in 1917 and is still well Case 5 was referred for treatment in 1917 after an operation in which all of the diseased tissue could not be removed The disease was proven microscopically to be malignant At the beginning of treatment there was general induration about the tissues of the neck and around the line of incision He was treated during six months when he appeared to be perfectly well He then discontinued treatment and passed from observation

He died in November, 1919, with evidence of metastasis in the spine. There was no local recurrence. Case 6 was treated in 1917. Within a period of two and a half years he had been operated upon four times for carcinoma of the thyroid and recurrences. Under x-ray treatment he showed some improvement, but died of mediastinal disease about six months after he was originally referred for treatment. Case 7 was referred for treatment in 1919 after exploratory operation in which a section was removed and the tumor found to be inoperable. Microscopical examination showed this to be carcinoma. Under x-ray and radium treatment he has finally recovered and is still well. Case 8 was operated upon by Dr John B Deaver for carcinoma of the thyroid and referred for post-operative treatment three weeks after operation. She was referred June 14, 1919, and was reported well September 9, 1921. Case 9 was referred by Dr H M Foss, who had operated upon the patient for carcinoma of the thyroid. The tumor was found to be inoperable and tissue taken for microscopical examination proved to be carcinoma. Treatment began September 10, 1919, the patient was still well September, 1921. Case 10, a female, age 68, was referred for treatment on account of an indurated, adherent tumor of the thyroid, which had all clinical appearances of carcinoma. She was first treated May 12, 1921, and was still well at the time of this report.

The following conclusions can be drawn. Every case of carcinoma of the thyroid that has been operated upon should receive as soon as possible at least two thorough courses of Roentgen-ray treatment and more if traces of the disease remain. If the diagnosis of carcinoma of the thyroid can be made without operation, a reasonably good hope of success from radiation treatment can be entertained. Recurrent cases can be made to respond to treatment and the recurrence can be made to disappear, but definite metastases are not likely to be controlled. Radium can be combined with the Roentgen-ray treatment to good advantage in carcinoma of the thyroid when the tumor has become definitely localized or when it ceases to respond to the Roentgen-rays—Author's Abst

(THYROID) Carcinomatous transformation of a lingual goiter
Ray (H M), Proc N York Path Soc (N Y), 1918, 18, 12-14

A brief report of a case of lingual goiter, which measured 5 cm in diameter. The tumor showed 'definite evidence of carcinomatous transformation'—J P S

(THYROID) Iodine and the metamorphosis of *Ammocoetes branchialis* into *Petromyzon planeri* Bloch (L'iode et la métamorphose de l'*Ammocoetes branchiales* en *Petromyzon planeri* Bloch) Rémy (P), Compt rend Soc de biol (Par), 1922, 86, 129-131

Experiments were made on ammocoetes. The larvae were kept in water containing iodothylin, or were given injections of iodothy-

rin, thyroid extract, emulsion of iodoform, etc. Apparently there were no cases of accelerated metamorphosis,—no silver color appearing in the ventral integument, or no appearance of eyes, which are the first stages in metamorphosis. Iodine, the accelerator of metamorphosis in batrachians, seems not to act as such on cyclostomes. Metamorphosis is regulated by a substance different from that of batrachians.—T C B

The modifications induced by **THYROID** treatment on the somatic structure in congenital sporadic infantile myxedema (*Le modificazioni prodotte dalla cura tiroidea sulla struttura somatica nel mixedema congenito sporadico infantile*) Rosso (M), Riv di clin pediat (Firenze), 1921, —, —, fasc 7, abst Terapia (Milan) 1921 11, 17

After careful observations the author came to the conclusion that the thyroid treatment in congenital sporadic infantile myxedema altered the megalosplanchnic growth of the patient into normal. The growth was in length, there was hardly any change in the transverse diameters. This result accords with what is thought nowadays about the morphogenetic influence of the thyroid secretion.
—G V

(**THYROID**) Goiter in relation to the trachea, especially from a tracheoscopic point of view. Schmiegelow (E), Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 26-31

The author mentions two cases in which a retrosternal goiter compressed the trachea. Tracheoscopy is helpful in the diagnosis of this condition, but in many cases radioscopy alone suffices.
—K H K

Diabetes with **THYROID** hypertrophy (*Sopra un caso di diabete con ipertrofia tiroidea*) Schupfer (F), Riv crit di clin med (Firenze), 1917, 17, 573, 586, 601, Pensiero med (Milano), 1916, 6, 547, 570

Reference verified from Index Medicus

Integumentary changes in the sheep following **THYROIDECTOMY** and administration of **THYROXIN** Simpson (S), Am J Physiol (Balt), 1922, 59, 445-446

Photographs of two rams were shown. Both were born May 7, 1920. From one the thyroid was removed at the age of five months, the other was kept as control. The horns were the same size in both at the time of operation. In November, 1921, in the thyroidectomized animal the left horn measured six inches, the right four inches. In the normal control the horns measured twenty-one inches. In a thyroidectomized lamb—a cretin dwarf—aged nine months thyroxin was given subcutaneously in half milligram doses

daily After a fortnight of treatment, although in the middle of winter in Western New York, the wool began to fall out, leaving the skin denuded When the amount of thyroxin was reduced a normal fleece developed Probably the original dose was excessive
—T C B

Blood flow and oxygen metabolism of the THYROID gland Knowlton (F P), Dooley (M S) & Curtiss (A N), Am J Physiol (Balt), 1922, 50, 446-447

The measurement of the blood flow and gaseous metabolism of the thyroid was undertaken with the hope that the method might be used to study the activities of the gland The method of Barcroft and Brodie was used The resting condition in dogs was studied The average result for the blood flow was 3.55 cc per gram per minute, for the oxygen consumption, 0.0927 cc per gram per minute
—T C B

(THYROID) The use of iodized table salt in the prevention of goiter Sloan (H G), Ohio M J (Columbus), 1921, 17, 172-174

After reviewing the general aspect of goiter prevention and the relation of iodine thereto, Sloan discusses methods of iodination of the body Iodine may be taken into the body by inhalation, by absorption from the gastro-intestinal tract or by absorption through the skin The need of iodine may generally be met by painting the skin with iodine, through the use of Syrup of Iron Iodide, one drop per year of age, daily during alternate months, or through sodium iodide in 0.2 gm doses, daily, for ten consecutive school days in the spring and autumn In the Swiss schools it has become a custom to suspend wide-mouthed bottles of iodine in the school room in order that the children may inhale the fumes Sloan points out that each of these is a troublesome method likely to be neglected until signs of thyroid enlargement actually appear To obviate this neglect, he recommends the introduction into all table salt of a small percentage of sodium iodide, one portion of sodium iodide to five thousand of salt is said to be sufficient to maintain a saturation of the normal thyroid gland which contains about 30 milligrams of iodine This practice, the writer believes, will eliminate goiter in the second generation At the same time it is not likely to affect badly either exophthalmic or mildly toxic goiters —J P McC

(THYROID) The surgical treatment of Graves' disease Soelling (H A), Hosp-Tid (Copenhagen), 1921, 64, Danish med Soc reports, 7-20

The author compares the results from about 100 cases of Graves' disease surgically treated, with other cases in literature In the acute cases (22) the results ordinarily were bad in both medical and surgical treatment In 90 chronic cases better results were

obtained from the surgical treatment than in 80 cases which were not operated upon. He has the impression that thymectomy is not advisable —K H K

Fibromyoma of the uterus accompanied by HYPERTHYROIDISM

Thompson (W H), Am J Obst & Gyn (St Louis), 1921, 2, 621-628

After reviewing the relations of the thyroid to menstruation and pregnancy, the author reports three cases suggesting to him that the hyperplasia and cell proliferation of the uterus found in fibromyomas may activate the thyroid, and that the myocardial weakness so often found with fibromyomas may be due to hyperthyroidism and not directly to the tumor —E N

The relation between food and THYROID Tsuji (K), Nihon Naikagakkwai Zasshi, 9, No 5, Abst, Jap Med World (Tokyo), 1922, 2, 45

The author previously dealt with a substance in raw cows milk which acted as a hormone on the thyroid. Egg yolk and butter caused an increase in the weight of the thyroid, and an increased function and histological glandular structure. Feeding with a mixture of pure albumin, carbohydrate, fat and salts caused atrophy of the thyroid with corresponding relative effects on other organs. He concludes that egg yolk and raw milk contain substances which stimulate the thyroid —R G B

Functions of the THYROID with special reference to the relation to diet. Tsuki (K), Igaku Chuwo Zasshi (Tokyo), No 352, Abst, Jap Med World (Tokyo), 1921, 1, 25

The author fed to animals food deficient in vitamins and observed their development and state of nutrition during the winter. Deterioration of, as extirpation of, the thyroid resulted in stunted growth or emaciation and a remarkable change in the alimentary and genital glands. Vitamin deficiency caused stunted growth or emaciation with deranged thyroid function, though it was still in an active state. The glandular organs underwent changes similar to those following thyroid extirpation. The author concludes that vitamins in the food has a hormone-like action upon the thyroid —R G B

(THYROID) A series of fifty cases of exophthalmic goiter treated by operation. Walron (A J), Practitioner (Lond), 1917, 99, 309-338

The importance of selecting a suitable time for operation to avoid exacerbations of the disease is emphasized. The technique of the operation is described in detail, special stress being given to control of bleeding. Post-operative treatment is then outlined, with

attention directed to the diet (following Ochsner's scheme) The author's mortality was 4 per cent Some of the patients have been followed for four years Of the 50 patients, 25 were completely cured, 17 were greatly relieved, able to return to work and normal living, but still showing signs of the disease, 4 were slightly relieved, 2 were not heard from after leaving the hospital, 2 died Brief records of the fifty cases supplement the article The author declares the surgical mortality much lower than that resulting from medical and x-ray treatment, which he places at 25 per cent Many of his patients had received non-surgical treatment for long periods of time prior to consulting him He is fair enough to recognize, however, that those patients who are cured or greatly improved by medical measures are not apt to come under the observation of the surgeon —H L

(THYROID) Further notes on the control of goiter in the new born
Welch (H), J Am Vet Assn (Ithaca), 1918, 53, 523-526

A report of experiences with congenital goiter in pigs, lambs, etc, in Montana and the remarkable beneficial effects of the administration of potassium iodide to mothers during pregnancy in its prevention It is recommended that two grains of potassium iodide be administered daily per animal, using sugar of milk as a vehicle, to be continued for 90 to 100 days This makes the cost of treatment about 50c per head He thinks the cost might be reduced, though the present figure seems low enough when compared with the results obtained —D M

(THYROID) Discussion on the medical and surgical treatment of Graves' disease
Wilhams (L), Proc Roy Soc Med (Lond), 1921, 14 (Clin Sect), 54

Writers are still far from unanimous as to which gland or glands of internal secretion are responsible for Graves' disease In a discussion on the medical and surgical treatment of Graves' disease at the Royal Society of Medicine, Wilhams contended that Graves' disease is not only not a hyperthyroidism but is not a disease of the thyroid gland at all He stated that the most outstanding feature of the complaint, namely, exophthalmos and cardiac troubles, are due to the implication of other glands, the exophthalmos being due to adrenal excess and the cardiac symptoms to enlargement of the thymus He considered that this enlargement, which occurred in 85 per cent of the cases, caused not only cardiac symptoms by pressure on the base of the heart and great vessels, but also many of the nervous symptoms by pressure on the vagus, sympathetic, and phrenic, as well as mental symptoms by interfering with drainage from the brain He regarded Graves' disease as due to toxemia in which all the members of the endocrine hierarchy are involved The only way of treating the disease, in

his opinion, is by discovering the source of the toxin and eliminating it. In a large percentage of cases the toxin is gastro-intestinal, and can be successfully dealt with only by dieting and, if necessary, intestinal antiseptics —Med Sci, 5, 300

Illustrative cases of malignant tumors of the THYROID Wilson (L B), Surg Clin N Am (Phila), 1921, 1, 1291-1306

Wilson believes that malignancy of the thyroid is of relatively frequent occurrence, that many cases start as adenomas in the third decade and progress slowly to malignancy. This long persistence, together with the resemblance of the tumor to other thyroid enlargements, is largely responsible for errors in diagnosis. Of 290 patients with malignant tumors of the thyroid seen in the Mayo Clinic during twenty years, 158 developed goiter before the age of thirty, 61 noticed thyroid enlargement less than a year before diagnosis, one-fourth had accelerated thyroid growth during the year preceding diagnosis, one-third had continuous growth for ten years. The author suggests careful histological examination of all nodular tumors, considering all markedly proliferating adenomas potentially malignant —C R

(THYROID) Graves' disease and manic-depressive insanity Wimmer (A), Bibliot f Læger (Copenhagen), 1919, 3, 262-278

We cannot necessarily conclude that there is an etiologic connection between Graves' disease and insanity in the cases where they are combined. The literature presents a great difference of opinion on this point. Many authors who have suggested "Basedowian insanity" have not considered sufficiently other etiologic factors (alcoholism, syphilis, etc). The connection is most probable in cases of delirium or confusion which may point to a toxic condition, but only a minority of the published cases of "Basedowian insanity" are of this kind. The most common insanity in Graves' disease is the manic-depressive type. Statistics, however, show that this combination must be regarded as only occasional. The author describes in detail 4 cases which point to the lack of constancy of the combination, especially, there is no connection between the time of incidence of Graves' disease and insanity —K H K

Phosphorus and ash content of the human THYROID (Sur la teneur en phosphore et en cendres du corps thyroïde du l'homme) Zunz (E), Réunion soc belge biol, 1920, 146-147

Analyses were made of 32 thyroid glands of average weight obtained from normal men killed in the war. The dry residue contained from 0.89% to 1.82%, av 1.38% P, and from 2.60% to 5.11%, av 3.86% ash. The ratio P/N ranged from 0.062 to 0.140, av 0.094. The ratio I/N ranged from 0.004 to 0.029, av 0.0154. The ratio I/P ranged from 0.025 to 0.422, av 0.1813 —Chem Abst

(THYROID, HYPOPHYSIS) A case of idioy de Vries (E),
Maandbl v Specialistische Geneesk (Amst), 1922, 5, 8

An idiotic girl of 19, of infantile type, has mammae somewhat developed and a pelvis of female form This is probably due to an endocrine disturbance, especially hypothyroidism and hypopituitarism —J K

Physiology of the TONSILS (Sulla fisiologia delle amigdale)
Farmachidis (C B), Riforma med (Napoli), 1921, 37, 923-924

After numerous clinical observations and a great deal of experimental research on the tonsils in regard to glycosuria, since 1914, the author comes to the following conclusions Acute pharyngo-tonsillitis may determine a transitory glycosuria Glycosuria can be evoked in animals by experimental irritation of the tonsils Ox tonsil extract shows glycolytic action even in vitro The glycolytic action is more manifest if the extract acts on glycose in urine rather than in distilled water Its action is demonstrable in glycosuric animals, even after removal of the pancreas Ox tonsil extract is antagonistic to the action of adrenalin The action is more evident if the extract is given intravenously Finally, Farmachidis claims that an efficacious action is obtained through tonsil extract in glycosuria as well as in the diabetic syndrome From these observations he infers that the tonsils are "among the organs apt to determine glycosuria through their alteration" and he thinks they are endocrine organs He quotes the experiment of Fleischmann (1921) The discussion is occasioned by the theory of infection through the tonsils, as published by Blodgett in Penn M J, 1921 —G V

The UTERUS as an endocrine organ (L'utero sede di secrezione interna) Fornero & Balli, Radiol med (Torino), 1921, Abst, Riforma med (Napoli), 1921, 37, 707

The authors claim that the uterus has a great endocrine value, they object to too hasty removal of the organ, on account of the consequent endocrine imbalance By x-ray treatment of the uterus they seem to have obtained renewal of uterine hormone production and correction of utero-ovarian insufficiency —G V

Endocrinology

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THE PRINCIPLES UNDERLYING ORGANOTHERAPY AND HORMONOTHERAPY

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Read at the Sixth Annual Scientific Session of the Association for the
Study of Internal Secretions, St Louis, Mo , May 22, 1922

INTRODUCTION

When we understand definitely what we are trying to do—and by this I mean having rather more than a vague general idea of desiring somehow or another to be of help to a sick person—we are more likely to be successful therapists than if we fumble about without plan in the hope of hitting luckily upon the right remedial agent. Much of our therapy is, it is true, empirical rather than rational, but we should know when we are working empirically and why, and we should strive to provide for our methods of treatment an ever more rational basis. We should, in other words, plan our treatments as far as possible in accord with *principles*, or *laws*, that we believe to be well established, or that seem likely to become so. There prevails a widespread feeling that many practitioners are making use of endocrine products in therapy in an indiscriminate and haphazard way, taking no trouble to ask themselves in a given case why the administration of such products may be indicated,

but administering glandular substances or derivatives, and especially "mixed products" in various abnormal states merely because advertising matter strongly commends their trial. In how far this feeling is justified by the facts, I do not know, though I fear that it is, at least to some extent, well founded. An extravagant use of these products must be hard to resist at a time when almost every layman has had his interest aroused in one way or another in the internal secretions, when even a considerable proportion of physicians hug the fallacy that because the myxoedematous child is backward mentally therefore most cases of mental deficiency can be cured if only the particular hormone that presumably has been lacking be administered, and when consultants are daily besieged by both laymen and physicians with requests to examine a great variety of patients who "surely must have something wrong with their glands." The situation is not at all surprising, considering the central place that in normal and pathological physiology, the endocrine activities have come, and rightly, to occupy. Giants and dwarfs, Basedowians and cretins, acromegalics and obese monstrosities, as well as eunuchs and pseudo-hermaphrodites are the victims of endocrine disharmonies. Many normal functions—visceral, neural, mental, metabolic—are demonstrably dependent upon certain secretions that are manufactured in and dispatched from the endocrine organs. An excessive production, a deficient production, or a perverted product may give rise to serious pathological states that sooner or later become manifest in recognizable clinical syndromes. Attempts to follow the trail back from the abnormal clinical picture through the altered structures and functions of the several bodily systems to the chain of hormonopoietic organs and beyond are laudable, but how difficult! Still, thanks to the steady, faithful work of clinicians, pathologists, experimental physiologists and biochemists, endocrinology is gradually being placed upon a firmer basis and we can begin to discern the single links in some of the pathogenetic chains. As a result of such work, a few principles useful as a guide to therapy can be clearly stated.

THE PRINCIPLE OF SUBSTITUTION IN ENDOCRINE DEFICIENCY

According to this principle, the therapist substitutes for deficient production of an endocrine product by a patient (1) an

organ derived from another person or from an animal that will steadily yield that product to the body of the patient (organ-transplantation), or (2) fresh or dried glandular substance derived from animals, or (3) the supposed active principle of the gland concerned, extracted from the glands of animals, or prepared artificially by the manufacturing chemist

Some of the greatest triumphs of therapy have been due to the application of this principle of substitution. I need refer only to our ability to control myxoedema and cachexia thyreopriva, either (1) by organ transplantation or (2) by administration of thyroid substance or thyroxin. Attempts at substitutive therapy in hypophyseal, parathyroid, suprarenal, gonadal, and pancreatic endocrine insufficiency have been less successful, though for each gland certain results have been achieved that encourage further work in the hope of discovering methods that will be more efficacious than any yet devised. The work of Toronto investigators on diabetes seems at this moment to be particularly promising.

THE PRINCIPLE OF MILD STIMULATION IN ENDOCRINE DEFICIENCY

The activity of a deficient endocrine organ can sometimes be increased by applying the principle of mild stimulation. We have reason to believe that the normal activity of secreting organs in general (inclusive of the endocrine) depends upon stimuli derived partly from the chemical substances in the blood and lymph, partly from the autonomic nerves. What physicians are accustomed to call "building up the general health," a therapeutic measure that all fall back upon for patients who are not well but whose condition does not yield definite indications for local surgical or chemical intervention, consists in altering the environmental influences (diet, fresh air, sunlight, exercise, massage, rest situation, including physical and psychological surroundings), in the hope of favorably influencing all the bodily and mental functions. In such a general reconstructive process, the physician applies the principle of mildly stimulating cells by increasing the adequate physiological stimuli that reach them.

Recently the attempt has been made to overcome endocrine insufficiency by mildly stimulating more directly the deficient organ by non-physiological irritants, such as x-rays or radium

emanations in small doses. This form of therapeutic stimulation has been tried in thyroid insufficiency, in hypophyseal insufficiency, in suprarenal insufficiency, and, recently, in insular insufficiency of the pancreas. It is too early, as yet, to judge of the efficacy of this form of treatment. The principle would seem to be a sound one, even though it should turn out to be of limited application.

THE PRINCIPLE OF ORGAN-REDUCTION OR OF FUNCTION-REDUCTION IN ENDOCRINE HYPERACTIVITY

In states of hyperfunction (and sometimes of dysfunction) of an endocrine organ, the therapist applies the principle of organ-reduction, or of function-reduction, often greatly to the benefit of the patient.

An organ may be reduced by partial excision by the surgeon, or by causing necrosis or degeneration of its cells by injections of hot water, by galvano-cautery, by electrolysis, or by intensive radiation with x-rays or radium.

The function of an overactive organ may be reduced by lessening its blood-supply (ligation of vessels, cold applications), by injury short of necrosis by means of x-rays or radium, by electrical treatment, or, sometimes, by a well-devised pharmacotherapy.

These principles of organ-reduction and of function-reduction have been successfully applied in the treatment of thyroid hyperfunction (Graves' disease, etc.), of ovarian hyperfunction (production of artificial menopause in severe menorrhagia and certain cases of puerperal osteomalacia), and of thymus hyperplasia (status thymicolymphaticus) and less successfully as yet in hypophyseal hyperfunction (gigantism, acromegaly) and in suprarenal hyperfunction (either chromaffine or interrenal).

THE PRINCIPLE OF UTILIZING HORMONES AS PHARMAKA IN THE TREATMENT OF CONDITIONS NOT NECESSARILY DEPENDENT UPON HYPOFUNCTION OF THE ENDOCRINE ORGANS THAT MANUFACTURE THEM

Physiologists, pharmacologists and experimental therapists are rapidly accumulating data that throw light upon the selective power of the several known hormones upon particular physiological mechanisms. The newer knowledge thus gained not

only gives us a better appreciation of normal endocrine functions than we formerly possessed, but in certain instances has placed in our hands for particular conditions new remedies whose favorable action could scarcely be accounted for by the assumption of a mere substitutive therapy that compensated for an endocrine deficiency. Thus the astonishing effects of epinephrin injections in bronchial asthma, and the equally remarkable results obtainable by pituitrin injections in diabetes insipidus and in dynamic ileus, to say nothing of its action on the uterus, are examples of the application of a new principle that may be capable of an unguessed extension. Is it not likely that, as medical science advances, we shall learn how to use as remedies a host of substances that we now know only as body-constituents of complex chemical constitution?

CONCLUSION

There are a number of other principles that endocrinologists are applying in their efforts at organotherapy and hormone-therapy. I should have liked to refer, had time permitted, to the principle of existing organ-deficiency as a favorer of successful organ-transplantation, to the principle of reciprocal interdependence of the endocrine organs as a basis for a stimulating therapy on the one hand and for an antagonistic therapy on the other, and to the principle of a multiglandular therapy in the management of generalized sclerosis of the endocrine organs. Time will not permit of this, however, and, moreover, as we know as yet but little regarding the last-mentioned principles, it seemed best to lay emphasis upon the principles that are better understood and are more generally applicable.

If physicians when studying the endocrinopathies will endeavor to make complete diagnostic studies before they plan their therapy, and if, when deciding upon treatment, they will keep in mind the therapeutic principles that may legitimately be applied in the present state of our knowledge of endocrinology, making use of the scientific imagination in devising better methods of application, they will be doing their best to secure all that is obtainable for their patients, to help their colleagues in the profession by extending knowledge and improving technique, and to protect their fellows as well as themselves from any deserved opprobrium.

A CHINESE CRETIN TREATED WITH NATIVE MEDICINE

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Cretinism among the Chinese apparently is not common. Annual reports from 14 hospitals in China, giving diagnoses of 33,000 in-patients, do not record a case of this disease.



Fig 1 A Chinese cretin, aged 17, after five weeks of thyroid medication. The attendant holds a meter stick.

The cretin here reported was a Chinese boy of 17 years who was sent to the Peking Union Medical College Hospital by Dr Bryan-Brown of the British Legation. There was no family history of goiter. He looked like a child of four or five years.

He could not walk without support and could answer only simple questions. His temper was uncertain. When displeased he squealed like a pig. He weighed 46 pounds and was 39 inches in height. His head was disproportionately large, eyes wide



Fig. 2 The same patient as in Fig. 1 after four months of intermittent medication consisting of turtle shell, tiger bone deer horn and thyroid. The Chinese doctor holds a meter stick.

apart, mouth open, lips thick, skin dry, and abdomen protruding. He had no axillary or pubic hair and the genitalia were infantile. There was persistent flexion of the wrists and fingers, in a position characteristic of tetany. Roentgenoscopy showed a bony development corresponding to about eight years. His blood Wassermann was negative, differential leucocyte count normal, blood pressure 85-60. Determination of the basal metabolic rate was not possible.

For a month before entrance the patient had been taking

three grains of dried thyroid gland a day without noticeable improvement. For the month that he was in the hospital he was given six grains daily. The resulting increase in metabolism was shown by an increase of the average pulse rate from 90 to 115, and minimum temperature from 97 to 98.6 degrees, by a loss of nine pounds in weight, and by a greatly increased output of urinary nitrogen and creatinin. Determinations on the urine were made by Dr. B. E. Read. Fig. 1 is a photograph taken at the end of five weeks of thyroid medication.

In spite of increased food intake the child continued to lose weight. He showed little or no mental improvement, and his father insisted on taking him home.

About four months later we were told that the boy was being treated by an old style Chinese practitioner and had shown remarkable improvement. Through the good offices of this Chinese doctor we were able to bring the boy, who lived in a nearby town, into the hospital for further observation. A photograph (Fig. 2) was taken of him and his doctor at this time. Examination showed that since discharge he had gained about 12 pounds in weight and three inches in height. His genitalia were more fully developed and the tetany-like contraction of his hands had almost disappeared. His father had taught him some acrobatic tricks and was greatly pleased with the physical and mental progress which he thought his boy had made. The medicine which the doctor prescribed consisted of a mixture of powdered turtle shell, tiger bones and deer horn. He had taken ten large doses of this, costing the equivalent of a laborer's wages for two months. During a part of the time he had also taken thyroid tablets given to him when he left the hospital. According to report, the Chinese doctor had gained considerable local fame for succeeding where the foreign doctor had failed.

McCarrison makes the statement (personal communication to Dr. J. C. Aub) that cases of cretinism with parathyroid deficiency do not improve on thyroid medication alone. In this Chinese boy parathyroid deficiency was suggested by the characteristic position of the hands. The question occurs, whether it is possible that the calcium in the bone prescribed by the Chinese doctor, supplemental to the thyroid gland given by us, produced a growth in bone and in genitalia and a quickening of mentality not secured by thyroid alone.

AN APPRAISAL OF OVARIAN THERAPY *

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INTRODUCTION

An appraisal of ovarian therapy, or of any other subject, must of necessity be tinctured with the personal element of the appraiser, so that it represents merely the point of view of an individual, based on such knowledge of facts as he may happen to possess. It presents more difficulty than does a mere survey of the literature, from which it differs to the same degree that the critique of a book differs from a mere synopsis of the book's contents. An accurate evaluation of such an undeveloped branch of therapeutics as that which forms the subject of this paper presupposes a finer judicial sense than the present writer can lay claim to. It is not easy to steer safely and sanely between the Scylla of over-enthusiasm and the Charybdis of undue skepticism. I may anticipate somewhat by saying that, of the two, Scylla looks much more dangerous to me than does Charybdis, to which I shall therefore be rather partial. One may be ever so enthusiastic as to future possibilities and yet be forced, in all honesty, to present a rather depressing picture as to what has actually been accomplished up to the present time by the therapeutic use of the various forms of ovarian extract. Since this paper is to be an appraisal and not a complete survey of the literature of the subject it can be kept within the limits of considerateness by presenting only the personal reactions of the writer, after a fairly abundant clinical experience and a reasonable familiarity with the literature of the subject.

HISTORICAL

The first attempts along the lines of ovarian therapy, so far as I have been able to find, were made at the Landau Clinic, in Berlin, in 1896, as detailed in several papers emanating from

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this clinic in that year. The first of these, by Manzer, (1), gives the credit for the idea to Theodore Landau. The method was obviously suggested by the good results which had been obtained from thyroid therapy, even at that time. Manzer reported the case of a girl of 23 in whom double salpingo-oophorectomy had been performed for extensive pelvic inflammatory disease, and who had developed severe vasomotor symptoms, which failed to respond to all ordinary methods of treatment. Ovarian therapy was then resorted to. Before the beginning of the treatment the patient averaged about twelve severe attacks per day of flushing of the head, giddiness, sweats, etc. Within three days of the beginning of the treatment, the attacks had diminished to a daily average of five. To make sure that the effect was not merely psychic, the patient received a substitute (scraped meat) on the seventh and eighth days, and felt much worse. On again being given the ovarian substance, improvement was again noted, to be followed by retrogression when the substitute was again given on the fourteenth day.

The preparation employed was the fresh ovarian substance obtained from the cow or sow. After careful removal from the animals, the ovaries were allowed to dry for twelve hours at a temperature between 60° C and 70° C, and then administered in the fresh condition. It was not long, however, before the substance was prepared commercially in convenient tablet form.

For a time the only preparation employed was that obtained from the entire ovary, but with the recognition of the corpus luteum as an accessory gland there were begun attempts to treat various conditions with preparations made from corpus luteum alone. Fraenkel (2) himself, the foster father of the general corpus luteum theory, reported good results in a small series of cases.

In 1904, Burnam (3) published the results of his observations on the use of fresh corpus luteum substance from the sow in the treatment of various gynecologic conditions. His results were so encouraging that a fresh impetus was given to this form of therapy. The literature of recent years abounds with reports concerning the use of both ovarian and corpus luteum substances in a great variety of conditions, as will be discussed below.

PHYSIOLOGICAL BASIS OF OVARIAN THERAPY

The known facts as to the physiological function of the ovary are sufficient to supply a logical basis for the general idea of ovarian therapy. Most of this evidence has been obtained, as with so many of the other endocrine glands, by studying the effects of ovariectomy in both human beings and lower animals. Much less impressive has been the evidence secured along positive lines, i. e., by studying the effects of feeding or injecting ovarian extracts of one form or another.

Whatever the relationship of the ovaries to the remainder of the endocrine chain may be, they are universally accepted as the organs which are directly responsible for the occurrence of menstruation. Furthermore, their removal is often followed by certain vasomotor and metabolic disturbances quite similar to those observed at the normal menopause. Again, the studies of Fraenkel, followed later by those of Meyer, Schroeder, Ruge, and others appear to have demonstrated conclusively that the corpus luteum is the element in the ovary which is responsible for the occurrence of the menstrual cycle, and the chronological relationships of the ovarian, endometrial, and menstrual cycles have been quite satisfactorily worked out. Far less satisfactory is the evidence concerning that function of the ovary concerned with general metabolism, that having to do with a possible influence on the growth and development of the generative tract and that pertaining to a protective influence on the early embryo. This is not the place to review these various questions, my object being merely to show the limitations of our present knowledge on these subjects as compared with the many therapeutic uses to which ovarian extracts are put.

PHARMACODYNAMIC ACTION OF OVARIAN EXTRACTS

Interesting observations have been made within recent years as to the effects of these extracts upon the genital organs. Adler (4) by the injection of watery ovarian extracts, and of ovarin (Poehl) into virgin rabbits and guinea pigs was able to produce changes similar to those normally occurring at the oestral epoch. Similar, though much less marked, changes were evoked by watery extracts of corpus luteum. Adler furthermore states that by administering ovarin he was able in two

cases to bring on the menstrual period, while the uterine mucosa showed the typical menstrual histological changes

Schickele's experiments (5) were perhaps even more striking. He injected extracts of ovary and of corpus luteum into castrated animals and was able to demonstrate within two or three weeks a pronounced redness and swelling of the vulva and vagina, with the appearance of a mucous discharge. Similar observations have been made by Marshall and Jolly. Aschner likewise obtained results with ovarian extracts while the use of corpus luteum gave negative results.

All the work thus quoted was based upon the use of aqueous or weakly alcoholic extracts of the ovary or the corpus luteum. To Iscovesco (6) belongs the credit of attempting to separate the active principle by the use of solvents which would not leave behind the lipoids, for he believes that the latter represent the biologically active principle of the secretion. Iscovesco's work marks the beginning of a really scientific effort to isolate the active principle of the ovary. He divided these lipoids into two groups, the homostimulating and the heterostimulating, depending upon whether they act only upon the organ from which they arise, or also upon the other organs. In the former group he places the secretions of the ovaries and of the testes. He was unable to distinguish any difference between the lipoids of the ovarian and corpus luteum extracts either physiologically or therapeutically. For the rather complex details of his method of preparation I shall refer the reader to his various papers.

A somewhat similar technique led Fellner (7), in 1912, to the isolation of a substance which produced striking effects upon the uterine musculature, epithelium and glands. These effects were noted even in castrated animals. Perhaps the most thorough and most suggestive work of this sort, however, has been that of Herrmann (8), published in 1915. This author believes that he has isolated the active principle of the ovary, and the illustrations accompanying his article, showing the effects of injection of the preparations, are certainly quite impressive. The technique he employs is a very complicated one, but its end result, Herrmann believes, is the isolation of the active lipoid principle, which he believes is contained in the corpus luteum. Incidentally he finds that the placenta contains identically the same principle. The lipoidal substance which he

has worked out shows a high grade of activity, but whether it is itself the active principle, or whether it merely contains the latter in a concentrated form, can not yet be definitely stated. Herrman's claim to priority in this matter has been challenged by Fellner, and an interesting controversy on this point has been waged in recent numbers of the *Zentralblatt für Gynakologie*

Finally, mention may be made of the investigations of Seitz, Wintz and Fingerhut (9), who separated from the corpus luteum two distinct substances which they call luteolipoid and lipamin. The former has an inhibitory action on the menstrual function and is found in large amounts in the later stages of the corpus luteum. The lipamin, on the other hand, is said to stimulate the growth of both the internal and external genitalia in animals, while its subcutaneous injection in amenorrhoeic women will bring on menstruation. Both of these substances have been prepared commercially in Germany. It may be added that the methods employed by Seitz, Wintz and Fingerhut in the preparation of these substances have been criticized by Heermann, who believes that the results obtained were incorrectly interpreted.

Aside from any possible specific effects of the administration or injection of ovarian extracts other phenomena have been noted which may have some bearing on the therapeutic employment of these substances. For example, Federoff, in 1899, found that an important effect of ovarian extracts was a slowing of the heart and an elevation of the blood pressure. The latter observation, however, is contradicted by most subsequent investigators. Goñalons (10) finds that "immediately following the injection of 20 cc of maceration or decoction of gravid corpus luteum, there is a rapid hypotension of 50, 60 or even 80 mm of mercury. The pressure falls rather rapidly, cardiac pulsations are generally considerably weakened, and there are sometimes in the first moments deep convulsive respirations. After 1, 2 or 3 minutes the pulsations strengthen and the pressure rises. This is relatively rapid at first. After 5, 7 or 10 minutes, sometimes more, the pressure returns to normal, at other times it persists a little diminished." Goñalons states that the same general results, though less marked, are observed if a maceration or decoction of the ovary is used. He finds,

furthermore, that both ovarian and pregnant corpus luteum preparations produce a tonic contraction of the uterine muscle, with also an increase of the rhythmic contractions. His results are quite similar to those obtained by Barry Stickel, on the other hand, states that the intravenous injection of ovarian extract yielded no results. Bell and Hick also got negative results from ovarian extracts upon the virgin uterus, but noted a stimulating effect upon the pregnant organ. Adler found that the administration of ovarian and corpus luteum extracts usually produces an increase of blood pressure, while Schickele obtained just the opposite effect, a fall in the blood pressure.

Mention may also be made of the experiments of Matsumoto and Macht (11), who found that "in all cases" both ovarian and corpus luteum preparations produced a powerful stimulation of the contractions and an increase in the tonus of the excised uterus. This effect was more pronounced with the corpus luteum extracts than with the ovarian. The authors very properly, however, warn against the assumption that these effects are specific in nature, for stimulation of the uterus was produced by practically every other gland or organ with which they experimented. They recommend as a test for corpus luteum preparations, the determination of this effect on the vas deferens of the rat, which they found to be very sensitive to the preparation. This test, as will be noted below, has been adopted by at least one manufacturing house, although its value as an index of specific therapeutic activity seems very questionable.

THE COMMERCIAL PREPARATION OF OVARIAN EXTRACTS

This brief résumé of the physiology of the ovary and of the pharmaco-dynamic action of its extracts leads to the question as to whether or not manufacturers have kept pace with the progress of laboratory investigators along this line, slow as this has been.

I have recently written to three of the largest manufacturers of ovarian extracts in this country, with the request that they supply me with a detailed account of the method employed in the preparation of the various forms of ovarian extract. This request was very courteously responded to by each of these manufacturing houses. I am sure that many of you will be

interested in these communications, which are therefore included below

Manufacturer A "We prepare our corpus luteum product from hog ovary glands, selected, collected and shipped in accordance with the following specifications

"The hog ovary glands are taken only from Government inspected animals. Immediately after the animal is killed, the glands are placed in a container containing crushed ice, during the period of collection. They are then removed to a cooling room and spread out in layers not more than an inch in depth, and are allowed to remain over night, until all animal heat is removed. These glands are then placed in a Sharp freezer and are frozen solid. They are immediately shipped to our plant, where they are thawed out and the skins and tissue are separated by mechanical means and the corpus luteum is reduced to a pulp. This pulp is placed on drying pans in a vacuum drier and the product is reduced to dryness at a temperature below animal heat, approximately 90° F. This material is powdered and compressed into tablets."

"At no time during the process of preparation is the material subjected to a temperature above animal heat, nor is it treated with solvents or chemicals, or modified in any way. It, therefore, represents as nearly as possible, the fresh animal gland."

"The whole ovarian material is prepared in the same way, with the exception that the entire gland is reduced to a pulp and the tissue and skin is not separated from the corpus luteum."

"Ovarian residue is the separated tissue and skin obtained during the process of preparing the corpus luteum. Otherwise, the ovarian residue is prepared in the same manner as is corpus luteum."

"The soluble extracts are prepared by extracting the powdered gland with an aqueous solvent and treating the clarified solution with protein precipitating agents, filtering off the solution, concentrating in vacuo, after removing every trace of the precipitating agents, until 1 cubic centimeter represents the water soluble extractive from 2 decigrams of the powdered substance."

"These products are also standardized physiologically by the Macht-Matsumoto vas deferens test, Journal of Urology, April, 1919."

Manufacturer B "We manufacture Corpus Luteum and Ovarian Substance from the glands of both hogs and cattle. The corpora lutea are removed from the glands and the remaining portion of the glands, sometimes referred to as residue, is mixed with glands that are without corpora lutea and sold as ovarian substance in powder and in tablets."

"Our method of handling the glands is to take them while perfectly fresh, free them from fat and connective tissues, mince finely and desiccate in vacuo at a temperature ranging from 85 to 105 degrees F. This low temperature prevents coagulation of the proteids and insures full therapeutic activity. After the glands are desiccated they are defatted and powdered."

"We offer the two preparations referred to in powder and in tablets. We do not make any liquid preparations of either the ovarian substance or the corpus luteum."

Manufacturer C "The whole ovaries, as dissected from the animal in the packing house, are frozen solid and sent to us in this form so that they reach us without decomposition. The slightest evidence of any decomposition, which is best shown by the odor, is sufficient to cause us to throw them away, as we cannot take any chance on preparations of this kind. On the whole, such glands reach us in excellent condition. As a matter of fact, we do not think they stay in frozen state for great lengths of time, but are shipped to us quite fresh and are frozen merely to be certain of their preservation during whatever time elapses between their collection and manufacturing work in our laboratories.

"They come both from cattle and from hogs. On reaching our laboratories they are first carefully inspected, then washed, and any extraneous tissue removed. Now if it is decided to make desiccated whole ovarian substance, the entire gland is ground to a fine pulp and carefully dried at a low temperature in vacuum drier. The dry material is then ground to a fine powder and stored perfectly dry in air tight containers, preparatory to its further use in capsules or manufacture of soluble extract.

"For the preparation of desiccated corpora lutea, these characteristic yellow bodies are carefully dissected from the rest of the tissue and then ground and dried in vacuum in the same manner as above. The portion of the glands which remains after dissecting out the corpora lutea is likewise dried in the same manner and constitutes what we designate as ovarian residue.

"While we know, from such experimental work as has been done, that ovarian substance and corpora lutea both produce very pronounced effects upon human beings, and are exceedingly useful in the treatment of a variety of diseased conditions, yet our knowledge of the active principles contained in these gland products is practically nil.

"Working somewhat along the same lines as that for the preparation of the active pituitary solution from the pituitary gland, we have developed some soluble extracts of ovarian residue, whole gland and corpora lutea. We have used for this purpose a process, whose general outline is as that given by the U. S. Pharmacopoeia for the preparation of Extract of Pituitary Gland. In short, it involves the extraction of the desiccated gland (and the finer it is ground the better), with water slightly acidulated with acetic acid, the coagulation of proteids which can be coagulated by heating to just below the boiling point of water, and careful evaporation in vacuum so that the final solution will represent about 5 grains of desiccated gland in each cc. This would be equivalent to approximately 30 grains of the original fresh glandular substance.

"It is rather an odd characteristic of these solutions that on chilling they frequently solidify to a transparent jelly. It seems that what

soluble organic matter is dissolved is of gelatinous nature, and though present in the liquid to an extent of not more than about 4% will rather easily gelatinize, especially if the solution is kept in a refrigerator

"These solutions, as we handle them, are then sterilized by filtering, first through a Berkefeld and later through a Pasteur filter, and immediately filled into ampoules

"We have convincing clinical evidence that a solution so prepared does possess to a remarkable extent the activity of the original desiccated gland—but we have a long way to go yet before we can say exactly what is the nature of the active principle that is so dissolved, or how much of the organic substance appearing in the solution is really active, and how much may be merely traces of inert material that necessarily accompany it"

From these letters it will be seen that the general method employed is about the same in the case of these three manufacturing houses. It is true that there are certain differences in the method of drying the product, as well as in the matter of defatting or degreasing. Manufacturer B states that "after the glands are desiccated they are defatted and powdered". No mention is made as to how the defatting is done or as to what if any solvents, are used for this purpose. In view of the work of Hermann and others, as described above, this may be a matter of no little importance.

Although I have not written to all the manufacturers in the United States, I understand that practically all of them resort to degreasing processes. This makes a finer and smoother product from a commercial viewpoint but there can be little doubt that it diminishes the therapeutic effectiveness of the preparation.

There are other possibilities of error in the manufacture of these preparations. The collection of these glands at the abattoirs is done by employees of the latter. In spite of the training, these men receive in the selection of material which will conform to the specifications of the manufacturers, mistakes frequently occur, although manufacturers appear to make a real effort to check up the material after it reaches them.

The question of dosage of these various preparations is still in a very unsatisfactory condition. Unlike the posterior pituitary substance, the thyroid, and the adrenal substances, there has as yet been no effort at standardization, so that, when prescribing these substances, we must proceed on the basis of what

the manufacturer tells us concerning his own product, *i. e.*, just how many grains of fresh or dried substance each tablet or capsule represents, and what the average dosage should be. This puts us in a rather unenviable position, with no relief in sight until some satisfactory basis of standardization is worked out. The physiologic test of Matsumoto and Macht, which at least one firm has adopted, impresses one as of doubtful value. While it may furnish a good index of the effect of the preparation in stimulating contractions in the excised vas deferens of the rat, it is by no means certain that it can be interpreted as an indication of the amount of specific corpus luteum secretion present in the product.

Equally unsettled is the question of whether the extracts, especially those of the corpus luteum, should be prepared from the ovaries of pregnant or of non-pregnant animals. Some manufacturers emphasize, as a special advantage of their product, that it is derived only from pregnant animals. Osborne (12), on the other hand, believes that, "for ordinary clinical purposes the mixed preparations from both pregnant and non-pregnant animals seem perfectly satisfactory." If the word "equally" be substituted for the word "perfectly" in the latter sentence, I should be willing to subscribe to it. It seems certain that there must be some difference between the effects of the corpus luteum of menstruation and that of pregnancy, but it is useless, in the present state of our knowledge, to speculate on the exact nature of this difference, and how it effects the pharmacologic action of the corresponding extracts.

FORMS OF OVARIAN EXTRACT AVAILABLE

A number of forms of ovarian extract are available commercially, so that one may prescribe according to one's views on the relative importance of the corpus luteum and other elements in the ovary. Extracts of the entire ovary, as well as those of the corpus luteum, are now procurable in a number of different forms, *viz.*, tablets, capsules, powder, and even solutions suitable for hypodermic administration. Of the solid preparations, it probably makes no great difference whether one employs the powdered form, capsules, or the compressed tablets. Osborne considers that the substance is best administered in the form of a powder, in capsules of the desired dosage. With regard to the

soluble forms of extract, the evidence would seem to indicate that they are far less efficacious. This statement is made on the basis of such experimental work as that of Aschner, Herrmann and others, on the probable lipid nature of the active constituent of the ovary. There is no really worth while evidence that a mere aqueous extract of either ovarian or corpus luteum substance contains any of the specific secretion of the organ, and, in fact, the evidence is opposed to this view. These extracts are now prepared by practically all the commercial houses, and they have achieved a wide vogue. Aside from the literature of these manufacturing houses, there is surprisingly little to be found as to the therapeutic results which may be expected from them. Recently, it is true, a number of reports have appeared with regard to the hypodermic use of aqueous corpus luteum extracts in the treatment of the vomiting of pregnancy. The few favorable reports on this subject, however, are of no particular scientific value, as will be discussed later in this paper, and it is quite possible that these preparations are inert.

The use of "ovarian residue" was recommended in 1919 by Graves(13). This preparation is made from that portion of the ovary remaining after removal of the corpus luteum. The reasons advanced for the use of this substance are not convincing, especially the importance attached to the so-called interstitial cells, which do not exist in the human non-pregnant ovary. Furthermore, the few reports of the clinical results which it has given are not especially convincing.

A rather disquieting development of recent years is the question which has been raised by Kohler (14), Esch (15) and others as to whether, with hypodermic ovarian therapy, we are actually concerned with the specific secretion of the ovary—or corpus luteum, as the case may be—or whether this form of treatment is merely a form of non-specific protein therapy. Esch emphasizes a fact which must have impressed all those who have been interested in ovarian organotherapy, *i. e.*, that the same extracts are recommended in diametrically opposite conditions, and that numerous satisfactory reports as to the results in these conditions abound in the literature. This is especially true of extract of the corpus luteum, which is recommended in such antipodal conditions as amenorrhea and excessive menstruation. The former is commonly looked upon as indicative of a

hyposcretion of the ovary, either primary or secondary, the latter, in its purely functional forms, as probably due to hypersecretion of the ovary

As every one knows, corpus luteum preparations have been used for many years in the treatment of amenorrhea and scanty menstruation, with varying degrees of success. The foundation of this therapeutic theory is, of course, to be found in the Fraenkel-Born theory of the corpus luteum causation of menstruation. Numerous reports are likewise to be found as to their employment in menorrhagic conditions. This method of treatment was probably at first purely empiric. When the function of the corpus luteum became better known, there were many who looked upon this structure as an inhibitor rather than a cause of menstruation. Hence there was some logic in the use of corpus luteum extracts in cases of uterine bleeding. The truth, of course, is a combination of the two divergent points of view. Menstruation cannot occur without the corpus luteum, which causes the hypertrophic changes of the premenstrual period. On the other hand, the actual bleeding of menstruation presupposes a cessation of this upbuilding function of the corpus luteum, as a result of the advent of some new factor, perhaps associated with the death of the ovum given off at the preceding ovulation.

Esch quotes the apparently paradoxical results obtained in various forms of menstrual disorders by the use of ovarian and corpus luteum preparations, and shows that this applies also to the results obtained by preparations from the pituitary body.

To make a long story short, Esch urges that the effects obtained by the parenteral (intramuscular) administration of the various forms of ovarian extract are probably of non-specific character, and that they represent, as a matter of fact, only a form of protein therapy. To substantiate this view, he treated a series of cases by the intramuscular injection of either breast milk or certain proprietaries (Aolan and Caseosan) of albuminous nature. His results were certainly as good as, or better than, those to be obtained with the use of organ extracts. This was particularly true of the cases of excessive menstruation. For his detailed results I must refer the reader to his two recent papers.

Enough has been said, I am sure, to make it plain that this

new aspect of the problem opens up many interesting possibilities. It is rather discouraging, after a quarter of a century of ovarian therapy, to have so fundamental a question as to its validity raised. The theory of protein therapy of this sort is that the effects are produced by the general stimulating action of the split products of the proteins along various lines—gland (and endocrine) activities, muscular action, etc. This work does not, apparently, attack the rationale of the ingestion method of ovarian therapy, except in so far as it creates doubt as to the presence of any of the specific secretion in the various commercial preparations commonly employed.

It is too soon to pass judgment on the correctness or incorrectness of these recent investigations. They strike a blow at the very foundation of ovarian therapy and emphasize again the importance of demonstrating beyond doubt the active principle of the ovary.

On the other hand, it may well be urged that the isolation of this principle should not be considered an essential for success in ovarian therapy. The results obtained from thyroid organotherapy were brilliant many years before the discovery of thyroxin by Kendall. A careful analysis of such a method of manufacture as that outlined by Manufacturer A in the above quoted letters fails to show any important defects. It would certainly seem that if there is any active principle in the ovary or corpus luteum, it would be kept intact by this method, which gives us the entire substance, without the removal of the slightest constituent by means of degreasing or other processes. If the whole product gives unsatisfactory results, is it probable that we would get better results from a purified ovarian extract, except perhaps in a quantitative sense? It would certainly seem that a carefully manufactured product including the entire corpus luteum substance, would contain the lipid substances to which such importance has been attributed by recent workers. The commercial preparation of extracts by methods similar to those employed in the laboratory by Herrman and others, methods which aim to get out the lipoidal constituents, would be a rather costly process. Perhaps it might be more feasible to make an oily extract which would contain many of these lipid principles.

From the fact that the results of ovarian therapy are so unconvincing even with the best commercial preparations, I am

inclined to believe that the real trouble is more deeply situated. We cannot even be sure that all the ductless glands have an appreciable amount of the active principle stored up within their cells. This doubt, it has always seemed to me, would apply with especial force to the ovary, which has to do with such purely vegetative functions as menstruation and reproduction. Or, the specific secretion may be present in some antecedent form which is in itself inactive. Finally, there is the possibility that it may lose its activity with the death of the tissue, or that it is destroyed by some of the essential steps in preparation, such as the drying or pulverizing process.

INDICATIONS AND RESULTS

It is unfortunate that most of the indications for ovarian therapy are of the subjective variety. Clinical results alone are obviously less reliable than would be the case if it were possible to control them by animal experimentation. The more conservative element in the medical profession has within recent years frowned upon the practice of proprietary medicine manufacturers of bolstering up their claims by means of "clinical reports" as to the therapeutic virtues of their preparations. However absurd these claims might seem to be, the graphophonic detail man could meet every objection by the stock argument that "after all, doctor, it is results that count." As if equally brilliant results could not be obtained, in many subjective disorders, by patent medicines of the most flagrant sort or by bread pills alone. The only difference between the innumerable patent medicine testimonials found in newspapers and many so-called "clinical reports" is that in the one instance the gullibility of the laity is displayed and in the other the credulity of the equally human medical profession. I trust that these remarks will not be misunderstood, for I am not discounting the unquestioned value of honest clinical observation carried out in a really scientific, truth-seeking spirit. To the clinician we are, as a matter of fact, indebted for some of the most important contributions to endocrinology. For the most part, however, we must look to the laboratory worker for the really substantial advances in this field of work.

Indications. Among the conditions for which ovarian extracts have been recommended may be mentioned amenorrhea,

functional uterine bleeding, dysmenorrhea, infantilism of the generative organs, the vasomotor and nervous disturbances of the menopause, sterility, obesity, repeated abortion, vomiting of pregnancy, pruritus vulvae, kraurosis vulvae, deficient mammary secretion, epilepsy, and Graves' disease. To these might be added quite a number of others even more illogical than some enumerated. Only a few of these have any claim whatsoever to serious consideration.

Amenorrhea The use of ovarian extracts would appear to be a rational procedure in the treatment of amenorrhea of the so-called functional type, especially that seen so commonly in association with the adiposo-genital syndrome. I have treated many such cases with extract of whole ovary and many with corpus luteum extract, and have not been able to convince myself that the patients have derived any very great benefit. This is especially true when these extracts are given alone, *i. e.*, when they are not combined with pituitary or thyroid extracts. In the latter case, I have at times obtained results which were at least encouraging. My impression, however, is that these same results would have been obtained had the ovarian extracts been omitted, and that the thyroid was the potent element in the treatment.

Aside from my personal experiences, I have been unable to find any reports in the literature which would convince me that this experience has been unique. Indeed, almost the only optimistic reports have been those embodied in the literature issued so generously by manufacturers of these preparations. The German school of gynecologists appears to have replaced ovarian therapy with pituitary therapy in cases of amenorrhea, as evidenced by such recent contributions as those of Kohler, Hofstatter, Fries, Zoppitz, and others.

In spite of the poor results which ovarian therapy gives in cases of functional amenorrhea, it is certainly to be preferred to the less rational, equally unsatisfactory, and more dangerous use of the emmenagogue drugs which have in the past been so popular (the vegetable oils, manganese, etc.). In many instances amenorrhea, in itself, calls for no treatment whatsoever, although it is at times difficult to convince patients of this fact. The laity, and to a less extent the medical profession, still seem to look upon menstruation as a means of ridding the woman's body of

noxious elements Furthermore, not a few women believe that amenorrhea predisposes to tuberculosis—that if a girl does not menstruate regularly she is likely to go “into decline” For this reason, an important part of the treatment of amenorrhea is to reassure the patient, to enlighten her as to the real significance of menstruation, and to impress her with the innocuousness of its absence, provided the amenorrhea is not secondary to some serious constitutional condition, such as tuberculosis or anemia

Uterine hemorrhage I have already referred to the fact that ovarian therapy is used in the treatment of both an absence and an excess of menstruation, and have discussed the reasons for this paradoxical practice As to the actual clinical results in cases of functional uterine bleeding, especially the hemorrhage of puberty and the climacteric, little of a definite nature can be said Good results have been reported by a few writers (Schroeder, Flatau, Hannes, etc.), but these reports are so few, in comparison with the great number of unsuccessful, and therefore usually unreported cases, that they must be received very unenthusiastically The form of therapy which has been perhaps most widely used for this purpose is the intramuscular or intravenous administration of the water soluble extracts In the light of what has been said above as to the questionable value of these aqueous extracts considerable doubt is thrown upon the occasional reports of good results following their use in cases of uterine bleeding Certainly uterine hemorrhage, in my own experience, is no less frequently benefited by the use of thyroid or pituitary extracts than by the use of either ovarian or corpus luteum substance

Menopausal vasomotor symptoms Here the indication for the use of ovarian extracts of one form or another is good, & c., it is based on known facts I believe it can be said that there is a nearer approach to unanimity among clinicians as to the value of ovarian therapy for this indication than for any other Whether, in the treatment of these disorders, ovarian or corpus luteum extracts actually do “hit the spot,” or whether we are here concerned with a great fog of self-delusion on the part of both patients and physicians, it is difficult to determine, through the very nature of the case The hot flashes, the flashes of heat, and the other characteristic symptoms of the menopause are purely subjective symptoms They vary much in severity

in different women, and in the same woman at different times. The duration of the menopausal disturbance also varies a great deal, some women being annoyed for only a few months, others for a good many years. It is obvious, therefore, that the greatest caution is necessary in drawing conclusions as to the value of any therapeutic agent for symptoms of this character. Unless I have been greatly deceived, I have seen genuinely good results from organotherapy in this group of cases. The symptoms have often appeared to be diminished, though rarely do they cease entirely. These results have been obtained even when reviewed in the light of such clinical checks as are open to us in the management of cases of this type.

Dysmenorrhea and genital hypoplasia (infantilism, etc)

The only type of dysmenorrhea in which there would seem to be any excuse for ovarian therapy is that associated with underdevelopment of the uterus. The latter condition is probably not a manifestation of primary hypofunction of the ovary. I do not agree with the assertion of Frank (16) that the pituitary has nothing to do with the causation of uterine hypoplasia. There is considerable evidence, both clinical and experimental, that it is concerned. It would be absurd to argue that the existence of such a relation is made doubtful by the mere fact that pituitary feeding does not give results in cases of underdevelopment of the generative organs—just as absurd as to claim that the ovaries have nothing to do with menstruation because ovarian extracts will not bring on menstruation in castrated women. The pituitary treatment, as a matter of fact, would seem to be a logical plan in cases of genital hypoplasia, with or without dysmenorrhea. Since there is also at least a secondary hypogonadism in such cases, ovarian extracts would seem to meet a definite indication. The fact remains, however, that the actual clinical results by various combinations of these two organ extracts are negligible, so far as I have been able to learn. I do not believe, however, that the poor results from this method of treatment are to be considered as reflecting upon the correctness of the theory upon which it is based.

The vomiting of pregnancy In 1916 Hirst (17) suggested the hypodermic employment of the soluble preparation of corpus luteum in cases of vomiting of pregnancy. His view is that "it is not unreasonable to suppose that there is sufficient absorption

from the corpus luteum of pregnancy to account for disappearance of nausea, especially when one realizes that the nausea begins to diminish at the time the corpus luteum has reached its acme of development." This explanation is obviously purely speculative. It is a good example of endocrinology of the less desirable sort. In spite of this fact the treatment based on this idea was gobbled up without question by a profession always hungry for something novel and at least pseudo-scientific. Although Hirst reports eighty per cent of cures in cases of vomiting of pregnancy from the corpus luteum solution, which he now advocates administering intravenously, these figures have not been borne out where the result has been properly checked, as in the recent report of King (18). Rongy and others have likewise reported disappointing results. My own feeling is that the method will soon be thrown into the rapidly growing endocrinological junk heap.

Sterility The results of the treatment of sterility by ovarian corpus luteum extracts have not been sufficiently good to commend them to most clinicians. Even when an occasional successful result seems to follow, it need scarcely be said that the greatest caution should be exercised in crediting it to the organotherapeutic measures employed. Fallenberg (19) has advocated large doses of the extracts, beginning with five grains a day and gradually increasing until at the end of a month thirty grains a day is being taken. The treatment, he believes, should be continued for one year.

The most successful cases, according to Solomons (20), are those in which menstruation is scanty. These are ordinarily instances of uterine hypoplasia, in which the ovarian therapy is most frequently combined with the administration of pituitary substance. In spite of sporadic and usually unchecked reports of success good results are not ordinarily to be looked for in the treatment of sterility by ovarian extracts.

Obesity of hypogenital origin Obesity is frequently observed in cases of hypogenitalism, especially at the menopause or after surgical removal of the ovaries. Here the indication for ovarian therapy would seem quite clear, but it is only fair to say that it rarely yields results unless combined with the administration of thyroid extract in which case the latter is undoubtedly the potent agent.

Other indications The numerous other indications for which ovarian therapy has been employed are scarcely entitled to serious consideration. In practically all cases what little evidence there is as to good results is clinical and subjective, and as a rule even this form of evidence is not imposing either in quantity or quality.

GENERAL COMMENTS

In judging the results of ovarian therapy, or for that matter, of other forms of organotherapy, most of us have unconsciously succumbed to the familiar "post hoc propter hoc" error into which it is so easy to slip. In connection with endocrinology some one has given an amusing illustration of the absurdities into which we are so easily led. If the administration of cascara relieves constipation, ought we to assume, inquires this philosopher, that the constipated individual is a sufferer from hypocascarism? Ridiculous though this seems, it represents exactly the method of reasoning employed by many of us when we leave good old mother earth to float dizzily through the cloudbanks of endocrinology. As our former president, Dr. Cushing, said in his address last year, "The Lewis Carroll of today would have Alice nibble from a pituitary mushroom in her left hand and a lutein one in her right, and presto! she is any height desired."

The real stumbling block to success in ovarian therapy, as will be gathered from what has already been said, is a much more material one than that just mentioned, having to do, so to speak, with a condition and not a theory. Nothing can be more certain than that removal of the ovaries brings about a cessation of the menstrual function and frequently the appearance of a characteristic grouping of symptoms. Equally certain does it seem to be that the symptoms of the normal menopause are due to the cessation of ovarian activity. It does not follow, however, that the feeding or the injection of ovarian extracts can replace the normal ovarian secretion, that it can restore the menstrual function and cause a cessation of the menopausal symptoms. The removal of the parathyroids, to select another example, produces tetany and death. The fatal result can not, however, be averted by the feeding of any amount of parathyroid substance.

There are a number of perfectly rational indications for the employment of ovarian therapy in which the actual clinical results are of no especial value. In spite of the confession of

unsatisfactory results embodied in this paper, I am frank to say that I employ ovarian therapy for certain indications because I believe it to be based on rational principles, and because it is reasonable to hope that the biological chemist will sooner or later succeed in giving us ovarian extracts which will really approximate in their effects the action of the ovarian secretion *in vivo*. This, after all, is the real crux of the situation as it now exists.

In conclusion, I may frankly admit that the skeptical tone of this paper reflects an attitude deliberately chosen at the outset. If there is any field of medicine in which a healthy skepticism is urgently needed, it is that of endocrinology, and more particularly that of endocrine therapy. Hyperskepticism is more to be desired than hyposkepticism, to parallel the language of the endocrinologist. The medical profession is, on this subject, now swayed by a species of mob psychology which has deprived it of its common sense and its reasoning powers.

Incalculable harm has been done by the trashy superficiality, the ignorance and, at times, the commercialism which are reflected in much of the enormous literature which has grown up, mushroom-like, within the past decade or so. Especially unfortunate has been the influence of several books published quite recently. The author of one of these sounds his theme in the preface of his book, when he states that "only by therapy and by the use of extracts of these glands can we be led to definite conclusions." Surely he lays himself open to the charge of plagiarizing from the detail man whom we have already quoted in this paper. It is not surprising that the book in question is full of pseudo-scientific jargon. Many examples of this might be excerpted, such as this:

"If these glands which are associated with the development of the genitalia should at any period overact along these lines the child is unconsciously affected and feels a sense of attraction towards the sphere of the organs which are stimulated. This is the explanation for the slighter or greater tendency to what are called manipulations by the fingers of the organs known as the genitalia."

This book, I may add, is intended for the medical profession, and not for the public.

Or listen to this simple explanation of the menstrual phenomenon, from the pages of another recent classic:

"The amount of post pituitary secretion reaches a certain con-

centration. This in turn stimulates the thyroid and adrenal medulla. They in turn activate the ovarian cells, which congest the uterine glands and lining membrane. The follicle bursts, the ovum is discharged and wanders, the uterus waits and wonders. Nothing happens, the curtain is lowered, the scenery is removed, the actors revert to civilian clothes. That is the story of menstruation. One sees it clearly as a play of an internal secretory syndicate."

The absurdities of the purely commercial literature with which physicians of the country are being deluged, by postcard and otherwise, would be equally humorous were it not for the sad reflection that they are being swallowed by at least a fraction of the profession. It is not to be wondered at that the medical profession as a whole is showing signs of nausea, and that many formerly enthusiastic amateur endocrinologists have cast aside the whole doctrine in disgust. "Love that is too hot and strong, burneth soon away."

We must resign ourselves to the fact that future progress in endocrinology, including, of course, organotherapy, will be a slow developmental process, as it has been in all other branches of medical science. It will mean a tedious search for truth on the part of many men in many lands. Each year will add a few nuggets of knowledge, and now and then a bigger find will spur all the searchers to renewed efforts.

It cannot be said that there has been any noteworthy advance in ovarian therapy in the quarter century and more which has elapsed since its introduction. This is especially true as applied to the preparation of the commercial extracts upon which the profession as a whole is dependent.

The stellar rôle in the future development of this branch of organotherapy will unquestionably be played by the biological chemist. The time will almost surely come when we shall be able to place in the patient's circulation the specific secretions of the ovary or corpus luteum, as we now can of the thyroid, and when we shall not be obliged to strain the imagination to see good results from ovarian therapy. For the present, it would seem that this Association should function along both positive and negative lines. Not only should it endeavor to stimulate scientific thought and investigation in the field of endocrinology, but it should assume the duty of clearing from the line of advance the cluttering overgrowth of pseudo scientific and commercial balderdash with which it is now choked. In the words of wise old

Marcus Aurelius, let our Association "Be like the promontory against which the waves continually break, but it stands firm and tames the fury of the water around it"

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SOME RECENT WORK ON INTERNAL SECRETIONS *

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The present day literature of endocrinology is very extensive. The bibliographic volume of the new edition of Beidl's well known monograph now runs to about five hundred pages. This includes in general only the more important contributions. Our own check list of endocrine articles for the year 1920 includes about twenty-five hundred, from nearly five hundred different periodicals, in a dozen or more languages.

Anyone with even a cursory knowledge of this literature must be impressed with the fact that it is extremely uneven in quality. A certain proportion of the articles are highly technical and of immediate interest only to the specialist. A larger proportion are articles of merely ephemeral interest, such as serve to ventilate the theories of the author or to assemble in a superficial way some of the pertinent evidence on topics of current practical interest. Between these extremes, however, is found a body of literature comprising several hundred articles a year that are of wide interest to practitioners and biologists. The difficulties confronting students in this field have been grossly under-estimated and much paper and ink have been wasted in the promulgation of immature or even fantastic literature which the actual known facts by no means justify.

Endocrinology has been in a peculiar sense an empirical field. Many of our conceptions have been obtained, not as in the case of various other fields of medical research, by induction from basic facts experimentally determined, but by observations of end results of disorders of endocrine glands, or by that most misleading of investigational methods, empirical therapeutics. There have been many attempts, however, to conform to the fashion of the times, to give a protective coloration of scientific rationalism to merely haphazard observations. I believe that much of the disapproval that has been visited upon endocrinology

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has been due to such precocious attempts at rationalizing our data when no adequate rationalization is possible

As recently pointed out elsewhere (1), the implications of some of the common assumptions in this field have not generally been faced. The number of true endocrine organs is problematic, but many have not hesitated to postulate the existence of at least nine. Moreover, it is assumed that any one of these organs can manifest conditions of normality, dysfunction, hyperfunction, hypofunction, dysfunction plus hyperfunction, and dysfunction plus hypofunction, i. e., six different functional conditions. The possible number of distinct combinations of all these factors is 6 to the ninth power, or 10,077,696. Of these, one is normality of all glands, hence, there are, in accordance with the assumptions made 10,077,695 possible endocrinopathies.

There are other assumptions commonly made, however, which serve further to complicate the situation. Thus, it is held that glands may function vicariously for each other, that they may stimulate each other, or that they may inhibit each other. To what extent such relationships might modify the basic combinations mentioned, imagination fails to suggest. Moreover, these combinations are presumably not static, but fluctuating. As a matter of fact, of course, the situation, even were our knowledge complete instead of fragmentary, could not be expressed by any such simple mathematics. The simultaneous operation of such variable factors could be determined only by differential calculus, and finally expressed in an inclusive formula by integral calculus (Timme). It is conceivable that our remote descendants may receive their medical and scientific information in such terms. Practically, however, our generation must be content with something very much simpler.

Such considerations serve to emphasize the complexity of the problems with which the endocrinologist is confronted and to indicate the futility of a large proportion of the superficial or imaginative out-pourings that have been accepted by an unfortunately large number as endocrine literature.

But difficult as are the problems, and slow as genuine progress has necessarily been, endocrinology has now reached a point where it must command the respectful attention of all well-informed physicians. The laity are becoming versed in the

“wonders” of endocrinology The physician must become informed as to the actual facts

Whether or not the pineal should be regarded as an endocrine gland is questionable It is commonly believed that a correlation between pineal tumors and somatic and sexual precocity, *i e*, macrogenitosomia praecox, is well established A critical review of the literature, however, shows but few indubitable cases It is quite possible that the peculiar manifestations of these few cases may be merely neighborhood symptoms rather than indicative of actual pineal perturbations Perhaps the most significant contribution to the problem of recent years has been made by Dandy of Baltimore After devising a new approach to the pineal which would involve a minimal amount of brain trauma, he found it possible to remove the gland from puppies and to keep these in apparently perfect health for months Neither the clinical history nor the autopsy disclosed any evidence that complete extirpation of the pineal gland affected the animals in any way

Feeding experiments have given ambiguous results Some authors have reported stimulation of the bodily and sexual development In a few cages of young breeding rats I noted that reproductive activity was somewhat depressed by pineal feeding The experiments, however, have not been carried to sufficient length to be of much significance It is quite possible that in this as in other cases the dosage factor may account for conflicting results It is known as regards some other organ substances that results may be diametrically opposed, depending upon the amount of substance given or the attendant circumstances

Our conception regarding the hypophysis have been somewhat unsettled recently by work in the laboratories, especially of Cushing (2) and of Camus (3) at Paris It has been widely held that the infantilism or sex depression often seen in advanced acromegaly and other disorders due to pituitary disturbances are ascribable to functional deficiency of the posterior lobe It has been quite convincingly shown, however, that fat dystrophy, diabetes insipidus and infantilism can be produced by relatively slight injuries of the tuber cinereum at the base of the infundibular stalk, without touching the hypophysis This obviously suggests that the symptoms that have commonly been ascribed to

posterior lobe deficiency are due merely to disturbance of the tuber cinereum

This conclusion is more or less supported by the fact that the true neural lobe, proper, has none of the morphological characteristics that are commonly taken to indicate secretory activity. The fact that extracts of this lobe furnish the active substance, pituitrin, is readily explainable on Herring's hypothesis that the secretions of the pars intermedia pass through the posterior lobe and infundibulum into the cerebrospinal fluid. Whether this substance is of physiologic or merely pharmacologic importance remains yet to be determined. On morphologic grounds it is probable that the physiologically active portions of the gland are those derived from the primitive pharynx, namely, the anterior lobe, the pars intermedia, the thin epithelial investment of the neural lobe proper and the recently described pars tuberalis, which extends upward along the stalk of the infundibulum.

Whether the neural lobe has any productive physiologic function or not, there is no doubt of the pharmacologic importance of its extracts, *e g*, pituitrin. These are widely used as smooth muscle stimulants, particularly in cases of uterine inertia in obstetrics, or in the prophylaxis and treatment of surgical shock and of intestinal atony with tympanites. The lack of toxicity of such extracts would theoretically render them preferable to ergot or eserine. Recently it has been claimed that pituitrin in repeated small doses can be used successfully to induce premature labor. Some practitioners hesitate to use the drug on account of its potency and the varying susceptibility of individual patients. It has been suggested that the danger can be eliminated by giving pituitrin on a bit of cotton held under the tongue, thus permitting control of its absorption.

The utility of pituitrin in the control of diabetes insipidus has become well established. In most cases, one to three doses of 1 cc each per day suffice. The benefit, ordinarily, is temporary, though recovery from the disease has been reported following its use. The experience of practically all previous investigators has been that the pituitrin must be administered hypodermically. Reese and Olmstead (4), however, working at the Barnes Hospital at St. Louis, have made the interesting discovery that pos-

terior lobe extract, when given by mouth in salol-coated capsules may control the disorder as well as do extracts given by injection

Both in the clinic and in the laboratories a great deal of work has been done of recent years to determine the usefulness or uselessness of anterior lobe preparations Goetsch's results from feeding pituitary substance to breeding rats have been widely quoted It was noted that those rats which received the anterior lobe substance showed more rapid sexual development and gave birth to more offspring than did the controls Goetsch's experiments, however, involved only a few animals and his controls were apparently not normally fertile The subject is still under investigation in several laboratories, the general trend of the evidence seems to support Goetsch's conclusions, though numerous negative results have been obtained

In practical therapeutics, desiccated pituitary substance is gradually gaining a recognized place Beck of Baltimore, Englebach and Tierney of St Louis, Timme of New York and others have obtained results in certain cases that are apparently incontrovertible In the light of this work pituitary substance is definitely indicated in the so-called girdle obesity, the type in which fat is found predominantly in the region of the hips In some cases, marked reduction of fat has been obtained, while in others, merely a redistribution to give a more normal body contour In such cases, Tierney recommends that pituitary substance be used alone, at least for a period of months until it has proved either inefficacious or until the initial improvement has come to a standstill Empirically, it has been found in the latter case that further improvement may be obtained by substituting thyroid substance Whether the anterior lobe or the whole gland preparations are used is probably of little moment so far as girdle obesity is concerned There is some reason to believe, however, that whole gland preparations have somewhat more extended usefulness than anterior lobe alone Various clinicians have reported, and my own limited observations have confirmed the impression, that whole gland material not infrequently produces a striking feeling of general well-being, which seems to be correlated with increased tonicity of the muscular tissues Observations of this sort are, of course, hard to evaluate on account of the difficulty of controlling the merely psychic aspects of the case It should not be forgotten, however, that changes in the

subjective feelings of a patient are important realities and are by no means always psychogenic. This is sufficiently demonstrated by the conversion of a thorough going pessimist to a sunny faced optimist within an hour by an effective dose of calomel.

In case of pituitary as well as other types of organotherapy, in the present state of our knowledge, it is desirable that single gland products be used in preference to pluriglandular formulas, unless the indications for the latter are very definite. The outstanding need at the present time is to determine the independent value of each substance. One need but recall the tremendous number of theoretically possible endocrinopathies to realize the dubiety of hit-or-miss gland mixtures. Even on a basis of mathematics alone, the probability of misses greatly exceeds the probability of hits. In any unanalyzed syndrome a random gland substance is quite as likely to do harm as good. In this, as in other fields of therapy, one should remember that the primary object of the detail man or of the commercial propagandist is to sell merchandise. After all, the seductive remark, "What do you care about science, Doctor, if you get results?" is an appeal to uncritical gullibility by which many a product of little worth has been foisted upon the medical profession. If it be a legitimate argument, the profession has no ground for objecting to chiropractic, Christian science, nostrums or numerous other irregular therapeutic agencies, because all of these "get results." Any doctor should know enough about placebos to appreciate the psychology of the situation. If he does not appreciate the futility of appeals to uncontrolled "experience" he should devote a few evenings to a good history of medicine. Despite the theories of certain enthusiasts to the contrary, centuries of experience have shown that the "therapeutic test," in itself, is a most prolific source of error.

As regards the thyroid, the more important data have been widely published. That the medical profession has not adequately assimilated these data, however, is obvious from the fact that many cases of thyroid deficiency go for long periods unrecognized. Rowntree recently mentioned a case of a physician who, within the past few months, was found at the Mayo Clinic to be suffering from well marked myxedema of years' standing. He had been under the treatment of excellent practitioners, but

none of these had recognized the obvious hypothyroidism from which he was suffering. In a recent study, Anders (5) found that in 55 cases of myxedema collected from the American and Canadian literature, 74 per cent had failed of diagnosis by one or more physicians. As diagnostic signs Anders lays special stress upon the firm, inelastic thickening of the skin and subcutaneous tissue that does not pit, together with the mask-like immobile features. The mucous membranes are often infiltrated and the teeth may become loose. The tongue, lips and nose are thick and the voice has a peculiarly monotonous character, though with frequent curious nasal explosions. Mentality is, in general, sluggish, though memory may be good. Scantiness and dryness of the hair are common. Albuminuria is frequently found. This fact often leads to a mistaken diagnosis of nephritis by those clinicians who have an exaggerated opinion of the importance of laboratory tests as contrasted with good clinical sense. In younger subjects there is one sign which, in the absence of syphilis, is practically pathognomonic,—that is, the saddle nose which results from unsymmetrical development of the cranium.

In view of the ease with which brilliant results may be obtained by thyroid therapy in these cases, it is unfortunate both for the patient and for the clinician himself when the diagnosis is missed. There is little need for laboratory tests in such cases, but basal metabolism determinations are of considerable use when the diagnosis is actually doubtful and when reliable determinations are available. Despite the usefulness of this test for orientation and control of therapy, its value is probably just now over-estimated by physicians generally. Even in borderline cases the test is not conclusive of thyroid disturbances since the metabolic rate may be influenced by various factors other than thyroid perturbation. Jones (6), moreover, has recently emphasized the fact that basal metabolism determinations frequently involve a much wider margin of technical error than is commonly supposed. Several other tests for thyroid disorders are now being studied, such as complement fixation, silver reduction and quinine tolerance, but the value of each remains yet to be determined.

One important aspect of thyroid work is that of Kimball and Marine (7) on goiter prophylaxis. Evidence is accumulat-

ing that there are several distinct belts of endemic goiter in this country, one of the largest being the Great Lakes region. A careful survey was made in the Akron schools both of the incidence of goiter and of the efficacy of iodine in its prevention. It was found that only a minute quantity of iodine need be given to prevent the development of the disorder. Thus it falls within the power of the medical profession largely or entirely to eliminate a disease which, while ordinarily mild in its manifestations, has numerous serious end results, either in the patient or the offspring.

The subject of parathyroid deficiency has been studied by several recent investigators. Paton and his collaborators at Glasgow found that in experimental parathyroid tetany there appears in the urine the substance, methylguanidine. This substance was found to increase nervous irritability. Chemically, it is closely related to creatine, which, in turn, is related particularly to muscle metabolism. Hammett (8), at the Wistar Institute, studied the incidence of tetany following parathyroid extirpation in rats. The mortality in case of 102 wild Norway rats was 90 per cent. In a large number of untamed, caged albino rats the mortality was 79 per cent. When, however, parathyroid extirpation was performed on similar albino rats that were used to being handled—"gentled" animals, as Hammett calls them—the mortality was only 13 per cent. The high mortality in the excitable rats Hammett believes to be correlated with the heightened neuromuscular activity, with resultant toxin formation. These observations have an interesting bearing on the use of sedatives, particularly of calcium salts, in the treatment of parathyroid tetany. It would seem probable that the beneficial effect is due, in part at least, to depression of neuromuscular activity.

More recently, the problem has been under further study by Dragstedt and Luckhardt (9) at the University of Chicago. These investigators have emphasized the importance of the alimentary tract as a source of toxin. What is of particular practical interest is their finding that the symptoms can be controlled by measures directed solely toward decreased formation and increased elimination of toxins. By withholding animal protein from the diet and by copious administration of fluids they were able to keep their dogs alive and free from tetany for a period of

a few weeks, after which therapeutic measures could be discontinued without unfavorable results. This would seem to indicate that compensatory adjustments had taken place. It also raises the question whether the favorable results reported by a few investigators from parathyroid grafts were not due merely to such adjustments rather than to any function of the grafts themselves. The Chicago investigators regard parathyroid tetany as closely resembling other types of tetany encountered in clinical practice and point the way to more successful therapy, that is, to eliminate animal proteins and to force fluids extensively, utilizing sedatives only to the extent that is necessary to supplement these measures during the acute phase of the disorder.

As regards the thymus, little need be said. Morphologically, it lacks the characteristics of a secreting organ. It can be removed in toto from young animals with no detectible disturbance of the body function. Moreover, contrary to common impression, the thymus gland is one which is proportionately largest at birth and constantly recedes in relation to body weight until puberty, when it, with other organs, ceases to grow. In short, the thymus, in all probability, is not an endocrine gland.

Research on the adrenals continues active. Space permits only passing mention of the fact that Cannon's emergency theory has recently received support from several sources and is, in my opinion, practically established. During the past two or three years extirpation of one adrenal in the treatment of epilepsy has had considerable vogue in Germany. Some writers hold that a beneficial result has been obtained, others, that the procedure is of slight or no value. There is little in the demonstrated physiology of the glands to serve as a rational basis for the procedure and the promise of the method would not seem to be sufficient to compensate for the potential danger involved. Of more immediate practical interest is the fact that several writers have recently reported that the administration of adrenal substance is of considerable value in the treatment of exophthalmic goiter. Shapiro and Marine (10) believe that best results are obtained with fresh gland substance. In a case which they recently reported, the dosage was 5 grams daily. Larger doses caused nausea.

Perhaps the most interesting recent development in the whole endocrine field is the work of Macleod (11) and his col-

laboratoirs at Toronto Many investigators have dreamed of the day when the supposed internal secretion of the pancreas might be obtained in an effective form for use in the treatment of diabetes Many experiments have been made in the attempt to obtain effective preparations, but with little success, apparently on account of the fact that the enzymes of the pancreas destroyed any hormone originally present in the pancreatic substance The Toronto investigators made use of the well known fact that ligation of the pancreatic ducts causes destruction of the enzyme-producing cells without causing diabetes and hence, supposedly, without interference with the endocrine function Pancreatic ligation was therefore performed on experimental animals and the atrophic gland remnants subsequently obtained and extracted Such extracts were found to produce a considerable lowering of the hyperglycemia characteristics of diabetes More recently, by special methods, it has been found possible to obtain effective preparations from normal pancreas material Studies are under way to isolate the "active principle" When this is obtained it may be identified chemically and synthesized artificially, as is adrenin

As regards the sex glands, recent work has mostly been in the hands of clinical investigators Corner has published several important contributions on the origin and morphology of the corpus luteum, but these are chiefly of technical interest Despite the widespread use of ovarian products in gynecology, clean-cut knowledge of their utility and of indications for their use is very slow in development Novak (12) has recently made a careful survey of the situation and finds it desirable to recommend a distinctly conservative attitude While brilliant results are occasionally reported in a considerable variety of conditions many failures have also been encountered Perhaps the greatest practical difficulty is the lack of standardization of ovarian products and, hence, of a definite base line from which to work To those who are especially interested along this line Novak's article is commended

As regards the male sex glands, the work of Sternach has aroused much interest together with considerable controversy, especially among German investigators Sternach's earlier findings that sex gland transplantation may result in striking modifications of morphologic and psychologic sex manifestations has

been confirmed, particularly by Sand (13) of Denmark and Moore (14) of this country. Hence, there is excellent experimental justification for clinical studies on the efficacy of sex gland transplantation. Experimental work indicates that best results are to be expected when host and donor are closely related. The clinical studies, especially of Laidston and of Stanley, have led to promising results. Despite the sensational publicity that this work has received, the problems involved are of sufficient importance to deserve extensive study at the hands of conservative surgeons.

More recently, Steinach has turned his attention largely to so-called rejuvenation studies. He has evolved a technique of ligating the vas deferens on one side and extirpating the epididymis on the other, with the idea of bringing about atrophy of the spermatogenic tissue and stimulating the nutrition of the interstitial cells. It will be recalled that essentially this operation has had considerable vogue in the past in the treatment of prostatic hypertrophy and that rejuvenation has not commonly been seen to result. Whether, as has been suggested, this is due to the fact that sufficient care was not taken to preserve the circulation remains to be determined. Sand (15) has recently reported very striking results from carrying out the Steinach operation on a senile dog. From a lethargic, feeble animal, the dog was converted into an active, alert individual that was able to accompany a bicycle rider in his pleasure excursions with evident signs of enjoyment.

So much for a hasty survey of a few of the results in case of the different organs. A recently introduced therapeutic procedure is worthy of brief mention, namely, that of stimulating depressed endocrine organs by light applications of x-rays. Not enough work has been done to permit any very satisfactory prophecy as to future developments, but some promising results have been reported.

Many writers have commented on the elaborate and somewhat awkward nomenclature that has developed in this field. Barker has recently proposed the adoption into English of a simple term that is gaining currency among German writers, namely, "incretion," comparable with "secretion" and "excretion." This usage would also give us the generic term, "incretory organs." The terms would seem worthy of general adoption.

In conclusion, I should like again to emphasize the fact that endocrinology, despite the world-wide interest that it has received for the past twenty years, is still in its infancy. The difficulties of investigation in the field have been greatly underestimated and many writers have given undue credence to much unreliable literature. This has led to the adoption of unfortunately extreme attitudes on the part of two groups of practitioners. The over-conservative group, who assume that the field is one merely of fantastic vagaries, overlook many substantial achievements and, somewhat wilfully, perhaps, fail to recognize that all of our knowledge of thyroid disorders and diabetes is a part of endocrinology. Their attitude, however, is more wholesome than that of the uncritical enthusiasts who assume a large body of well substantiated fundamental facts that do not exist.

It is only by careful, exacting study on the part of both practitioners and of laboratory investigators that the host of outstanding problems are to be solved. The situation calls primarily for earnest stick-to-itiveness, conservatism and whole-hearted support of proper studies upon the part both of clinicians and of experimental biologists. At the recent meetings at St. Louis the feeling was strongly in evidence that our problems are important, but that progress in their solution must be necessarily slow. Neither undue enthusiasm nor undue pessimism are conducive to the best interest of patients or of practitioners.

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CONCERNING THE PATHOGENESIS OF THYROTOXICOSIS PART I

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INTRODUCTION AND CONCLUSIONS

The "hyperthyroidism theory" of Graves' disease, which dates from 1884, is commonly accepted at the present time. It explains thyrotoxicosis as the antithesis of myxedema and is supported by several striking arguments. However, complete belief in this pathogenic theory has been precluded by certain conflicting data such as the frequent existence of hypo- and hyperthyroid symptoms in the same individual. During the thirty-five years since the conception of this theory, the development of our knowledge of thyroid pathology, physiology and metabolism has, especially during the past decennium, rapidly advanced, bringing to light additional facts which demand a renewed consideration of the pathogenesis of thyrotoxicosis.*

In the present article, after a brief survey of the older theories of Graves' disease, a critique of the hyperthyroidism theory is given from various viewpoints.

The facts and arguments in favor of the dysfunctional or dysthyroidism theory of thyrotoxicosis are then presented in detail. It is believed that the phenomena of Graves' disease can be most adequately accounted for on the basis of abnormal metabolic processes in the thyroid gland producing toxic effects upon the various tissues and organs, together with the systemic results due to lack of adequate amounts of the normal thyroid hormone.

More than the present knowledge of the chemo-physiology of the endocrine organs as well as of cellular metabolism is, however, necessary before we may arrive at a complete and ultimate understanding of the pathogenesis of thyrotoxicosis. Much must still be learned of the factors controlling thyroid secretion, of the intermediate steps in the synthesis of thyroxin in the human organism, of its exact chemical function and reactions in the

*In the present article the term thyrotoxicosis (Plummer) is used generically to include all local and constitutional manifestations of thyroid toxemia, including Graves disease so-called hyperthyroidism, toxic adenomata, etc.

repair and replacement of protoplasm as well as the exact relationship of the thyroid to other ductless glands. So many new data yet require to be obtained and duly correlated that a very conservative attitude seems indicated at present.

REVIEW OF THE THEORIES OF THYROTOXICOSIS **

The Detoxication Hypothesis After Moebius had called attention to the predominating rôle played by the thyroid gland in the production of the symptoms of Graves' disease, Notki, followed by Blum, evolved the detoxication hypothesis. The thyroid was regarded as serving to rid the body of certain toxins. The symptoms of Graves' disease were said to develop as a result of imperfect detoxication due to a pathologic thyroid gland. With the later recognition of the internal secretion of the thyroid and the necessity of this secretion to maintain cellular nutrition, growth and development, this hypothesis became untenable.

The Toxic Hypothesis Attempts have been made to show a relationship between a chemically altered water supply and thyrotoxicosis in a manner parallel with the supposed production of endemic goiter by water of high calcium content etc. Further study, however, showed that exophthalmic goiter is not an endemic disease and it is now known that the presence of bacterial toxins and not a changed chemical constitution in an effected water supply is necessary for the production of endemic goiter (McCarrison). The toxic hypothesis is regarded as disproven.

The Infectious Hypothesis This hypothesis gained some headway during the period of development of bacteriology of infectious diseases, having been supported by Virchow, Kocher and others. The hyperplasia and other changes were regarded as due to direct bacterial invasion. Extended investigation demonstrated, however, that thyrotoxic as well as other goiters are sterile. Again, evidence in abundance was adduced from the surgical side showing that thyroid hyperplasia also developed as a compensatory process after partial thyroectomy [Halsted (1) *et al*]. The older infectious hypothesis of Graves' disease should not be confused with the modern view of the production of endemic goiter through toxemia of intestinal and probably ultimately bacterial origin (McCarrison).

**The older literature on thyrotoxicosis is given in Moebius, P. J. *Die Basedowsche Krankheit* 'Wien, 1906, Hölder, and Sattler, *Die Basedowsche Krankheit* 'Leipzig 1909 Engelmann.

The Neurogenic Theory This theory relegates the cause of thyrotoxicosis to the central or peripheral nervous system as opposed to the "thyrogenous theory" in which the origin of the disease is regarded as being in the thyroid gland itself. Together these two theories and their modifications are the only ones receiving serious consideration at the present day.

The neurogenic theory is supported by older as well as certain new data. Charcot, Marie, Gauthier, Troussseau, Gerhardt, *et al*, regarded exophthalmic goiter as a disease of the entire nervous system, calling especial attention to the symptoms and signs of increased central, peripheral and vasomotor stimulation present.

This theory then developed in two divergent ways, one school emphasizing lesions in the central nervous system, particularly the medulla, the other, in the autonomic.

The Bulbar Theory was ably supported by Sattler, an unusually thorough student of Graves' disease. Sattler inferred from the frequency with which the cardinal symptoms, goiter and exophthalmos, were associated, that pathologic processes in the medulla or in still higher portions of the central nervous system must be present. The well known experiments of Filehne (2), corroborated by others, showed that on sections of the *corpora testiformes* of rabbits, exophthalmos, thyroid hyperemia and tachycardia occurred. Unilateral bulbar lesions produced such symptoms on one side only. Sattler also calls attention to the cranial nerve palsies, which sometimes are met with in Graves' disease, also the glycosuria and speech defects, as possible bulbar symptoms. The muscular spasms, contractures and paralyses can also be accounted for by the bulbar hypothesis (von Leube).

Other adherents to the neurogenic theory regarded the *peripheral* nervous system, particularly lesions and degenerated areas in the cervical sympathetic ganglia, as responsible for the disease. Thus, lesions in the upper cervical ganglion would effect motor and secretory cells in the muscle of Mueller, the thyroid and heart, in the median ganglion, the thyroid and heart, in the inferior, the heart alone. Eppinger, Falta, Rudinger (3) and Eppinger and Hess (4) have supplied many experimental and theoretical data in support of this view. Its most enthusiastic adherents maintain that Graves' disease with fully

developed sympathicotonic symptoms is necessarily due to the above origin

Support of this viewpoint from the pathologic side has been supplied by L B Wilson (5), who showed that experimentally produced lesions in the cervical sympathetic ganglia may cause histologic changes in the thyroid paralleling those found in the exophthalmic goiter. Wilson concludes that the thyroid is stimulated to abnormal function usually as a result of local infection in the cervical sympathetic ganglia. Cannon and Cattell (6) have also recently demonstrated the activation of the thyroid to secretion by the sympathetics.

Criticisms of the Neurogenic Theory The neurogenic theory properly emphasizes the importance of the nervous system in the pathogenesis of thyrotoxicosis. It has, however, proven inadequate to withstand various criticisms which will now be mentioned.

From the clinical standpoint, the presence of an irritative ganglionic lesion is usually assumed to account for the exophthalmos (contraction of the Muellerian muscle) and tachycardia (stimulation of the cardio-accelerator fibers). But how account for the thyroidal hyperemia and hyperplasia, which are best explained by a paralysis of the vasomotor fibers and a direct metabolic stimulation from the blood stream (example, increase in the goiter and clinical symptoms due to iodine administration)? The absence of pupillary contraction and presence of dilatation which actually occur in exophthalmic goiter would make it necessary to accept a selective stimulation of certain autonomic fibers and paralysis of others, which is paradoxical and does not merit credence. Murray pertinently remarks that irritative cervical sympathetic lesions in order to account for the symptoms must necessarily be regarded as persisting for many years in most cases, which is inconsistent with the usual reactions of neuroganglionic tissue to pathological stimuli. Filehne's rabbit experiments, in which certain symptoms of Graves' disease were produced, have also been criticised by Marie, who declares that such are no more Graves' disease than is the glycosuria produced by bulbar puncture to be regarded as true diabetes mellitus. [See C P Howard's (7) excellent critique of the Neurogenic Theory.]

Pottenger (8), a close student of visceral neurology, has recently emphasized that many thyrotoxic symptoms are actually

parasympathetic in origin, viz Von Grafe's sign, Dalrymple's sign, epiphora, sudorrrhea, diarrhoea, hyperacidity and eosinophilia. The neurasthenia, change of psyche, and tremor are to be regarded as of central origin. The nervous stimulation is, therefore, considered a general one involving in varying intensity the several portions of the nervous system, central, peripheral and vegetative, and consequently not confined to the sympathetic ganglia.

We have, furthermore, direct clinical evidence that *thyrotoxicosis can arise without primary involvement of the nervous system*, in those cases in which the disease has developed as a direct sequela of acute thyroiditis or as result of trauma to the thyroid.

From the pathological side there is also serious objection to a purely neurogenic theory. Many careful autopsies on patients dying of exophthalmic goiter have failed to demonstrate the regular occurrence of lesions in either the medulla or the cervical sympathetic ganglia. Again, bulbar disease with demonstrable pathologic changes is not found associated with the symptomatology of thyrotoxicosis more often than can be regarded as mere coincidence, although, according to the bulbar hypothesis, the reverse should be true.

The chief question in point, it would seem to me is whether Graves' disease arises endogenously in the thyroid gland itself or from neurogenic cause. An *exclusively* nervous origin of the disease is untenable as it has been demonstrated in many thousands of cases that the surgical removal of the major part of the thyroid gland is usually followed by subsidence of the signs and symptoms. From this general experience, the deduction is irrefutable that whatever indirect influence the nervous system may have in the production of the disease, the same evidently originates as a result of pathological changes in the thyroid itself. Persistence of the symptoms after thyroidectomy can be explained by pathologic and metabolic changes in the portion of the thyroid remaining after operation, together with permanent lesions in various organs due to previous effects of the thyrotoxic condition.

On the other hand, it is impossible to deny the marked influence of the nervous system, especially in those cases of thyrotoxicosis developing suddenly after fright and various other forms of mental shock. Cannon's recent demonstration of the

influence of psychic states and adrenalin upon the secretion of the thyroid secretion emphasizes the intimate relationship of the thyroid to the nervous and endocrine systems

In résumé, then, of the value of a purely neurogenic theory of thyrotoxicosis this theory may be dismissed as untenable in view of present evidence without, however, recognizing that the fundamental metabolic disturbance in the thyroid gland in this disease may be set up and largely influenced by psychic, trophic and endocrine factors under nervous control, also that toxic products of thyroid metabolism selectively attack nervous tissue

Critic's (9) *Kinetic Hypothesis* may be briefly mentioned in connection with the neurogenic theory This distinguished surgeon endeavors to correlate the nervous symptoms and lesions with those of the thyroid gland by regarding the disease as one affecting "the motor mechanism of man, the same mechanism that causes physical action and that expresses the emotions" "A pathological reaction" between the brain and the thyroid is produced by various nervous factors causing the disease to develop The arguments advanced in favor of this rather nebulous hypothesis are not capable of exact critical analysis

THYROGENIC THEORY

The Hyperthyroidism Theory of Thyrotoxicosis If then a purely neurogenic origin of the disease is discarded, the cause must be sought in the thyroid gland itself The *thyrogenic theory* is capable of two chief conceptions, the "hyperthyroidism theory" which ascribes Graves' disease to hyperfunctional condition of the thyroid as opposed to a "dysfunctional" or "dysthyroidism" state in which the secretion of the gland is regarded as qualitatively altered At present we are concerned with the pure "hyperthyroidism theory"

This view was first promulgated in 1884 by Rehn (10), although it is generally first ascribed to Moebius (11) (1886), who, however, while emphasizing the importance of the thyroid in the causation of exophthalmic goiter regarded the disease as due to increased but qualitatively altered thyroid secretion Eminent students of the disease soon accepted this standpoint in principle, although from the first many have adhered to the dysfunctional theory Among those who have supported the hyperthyroidism theory are Kocher, Reverdin, Gauthier, F Kraus, Falta, L B Wilson, Plummer

The chief data supporting the hyperthyroidism theory are the following

- 1 The thyroid tumor and histological evidence of hyperplasia
- 2 Relief or cure of the disease by thyroidectomy
- 3 Experimental production of hyperthyroidism in man and animals by thyroid medication
- 4 Increase of symptoms of thyrotoxicosis on exhibition of thyroid preparations
- 5 The contrast shown by the symptoms and signs of "hyperthyroidism" and hypothyroidism (Kocher) as well as by the metabolism

The hyperthyroidism theory is therefore apparently based upon some of the best known facts pertinent to thyrotoxicosis. The clear explanation of the morbid picture afforded by this pathogenic conception has greatly aided its general acceptance up to the present time. As so frequently experienced in the difficult science of medicine, a definite explanation of otherwise a peculiarly confused clinical picture is so attractive that even an array of other facts irreconcilable with such a simple theory are often overlooked or disregarded by most physicians. The inadequacy of the hyperthyroid theory to account for present knowledge of thyrotoxicosis can best be shown by criticising *ad seriatum* the above mentioned arguments supporting this etiologic hypothesis, prefixing such criticism with important *a priori* grounds for questioning the same.

CRITICISMS OF THE HYPERTHYROIDISM THEORY

Criticisms on a priori grounds If viewed from a broad physiological viewpoint, it is questionable whether the conception of "hyperfunction" has a sound basis, however convenient and ingenious it may be. We may seek through the whole realm of organology without finding a single instance of an idiopathic hyperfunctional condition such as is claimed for the thyroid in Graves' disease. Hypertrophy, hyperplasia and hyperfunction only ensue under normal conditions when there is a cause and demand for such a reaction either by additional functional strain on a normal organ or through depression of normal function through disease. For example, the heart of the mountaineer hypertrophies and increases its power through circulatory

stimuli produced by the higher altitudes. Again, cardiac hypertrophy results from hypofunction due to toxic degeneration of the myocardium. Acromegaly might be advanced as an exception to this rule, but even here the excessive overgrowth is asymmetrical and abnormally confined to the jaws, hands, feet, etc. It is accompanied by decreased physical and psychic vigor and general degenerative processes. This antithesis is so marked that the most eminent students of pituitary disease, including Cushing, do not accept a "hyperfunctional" condition of the hypophysis. Indeed, it is very questionable whether the general credence given to the conception of hyperfunction as applied to various endocrine diseases or symptom complexes, including exophthalmic goiter, is justified by present knowledge. There are many more current beliefs in modern clinical medicine which are generally held without scientific foundation or substantiation.

The function of the thyroid gland is largely one of control of growth and development. In cretinism both are markedly deficient. If, then, we unreservedly accept the "hyperthyroidism theory" of Graves' disease, we must regard the thyroid in this condition to be in a state of continual hyperfunction. If cretinism is the antithesis of Graves' disease, then we must needs expect a state of over-growth and over-development to be found in young thyrotoxic subjects, while actually there is no true over-growth and at times slight signs of retarded development. The elongated limb bones observed in cases of youths suffering from Graves' disease have been erroneously regarded as evidence of over-growth, whereas this phenomenon is actually due to the delayed sexual maturity (failure of gonadal stimulation of closure of the epiphyses).

Pathological Evidence The presence of hypertrophy of the thyroid gland in thyrotoxicosis has been used as one of the chief arguments for accepting an overfunction or overproduction of thyroxin as the cause of this disease. According to this view, the degree of hypertrophy present should be found to vary directly with the severity of the clinical symptoms. This, however, does not hold true. Some large goiters are accompanied by slight symptoms and conversely a very small goiter may be present in a very severe case of Graves' disease. Certain individuals show even marked symptoms without demonstrable thyroid hypertrophy.

Exophthalmic goiter is believed to follow great nervous and physical exhaustion or shock. It also occurs during or as a sequela to acute thyroiditis of bacterial origin, also various acute infectious fevers. In these exhaustive and depressing conditions, it is paradoxical to accept etiologically a hyperfunctioning organ which would actually demand unusually good, not poor, nutrition. In particular, it seems to the writer that the development of thyrotoxic symptoms in the course of an acute thyroiditis demands for their explanation, the recognition of morbid metabolic processes due to actual pathologic lesions in the secreting tissue, which a hyper-secretory hypothesis could but lamely explain.

Reasoning logically, one should expect marked hyperplasia of the thyroid to be regularly accompanied by the symptoms of thyrotoxicosis and conversely thyrotoxicosis to be as routinely associated with hyperplasia. In testing this assumption, we may refer to the most extensive and accurate pathological researches on goiter of the Mayo Clinic. According to Wilson's (12) and Plummer's (13) careful studies nearly all thyroidectomized patients had hyperplastic thyroids, but hyperplasia evidently does not necessarily lead to exophthalmic goiter, for of the non-hyperplastic goiters removed, 23.3 per cent were from patients showing thyrotoxic symptoms. Plummer (14) has, of late, remarked, "Areas of hypertrophy, 'some hypertrophy' (MacCarty), are present in such a percentage of all thyroids resected that this degree of hypertrophy has little, if any, tangible significance. In exophthalmic goiter, diffuse hypertrophy of the thyroid is rarely absent, but even in severe cases it varies from the most marked degree to the vanishing point." According to Boothby's (15) recent statistical report of 1,656 cases of goiter with histological studies, 254 were classified as non-toxic adenomata, i. e., as hyperplastic goiters without toxic symptoms, and 366 as toxic adenomata accompanied by thyrotoxic symptoms. Boothby states, "The pathologist, however, cannot distinguish adenomas which produce hyperthyroidism from those which do not." It is also shown from the numerous cases of this clinic that at least 16 years elapse from the development of adenoma to that of the appearance of thyrotoxic symptoms in the same individual. Maine and Lenhart (16) have also shown that there is no constant relationship between the degree of hyper-

plasia and the cardinal symptoms, exophthalmos and tachycardia. These authors also emphasize that hyperplasia is very common in simple goiters and other types of thyroid disease in which thyrotoxic symptoms are absent.

It follows from these amply demonstrated facts that the presence of thyroid hypertrophy and hyperplasia can have no direct etiologic bearing on the production of thyrotoxicosis, for hypertrophy and hyperplasia may be present without the development of thyrotoxicosis, the reverse may also be true.

Surgical Evidence A chief argument for the acceptance of the hypothyroidism theory has been the fact that surgical removal of the major part of the hyperplastic thyroid gland usually leads to cessation of the symptoms. This argument loses its apparent conviction, now that it has been shown that thyroid hypertrophy and hyperplasia cannot *per se* be responsible for the disease. Another explanation must be found for the hyperplastic processes in various thyroid diseases, including thyrotoxicosis (See below).

The surgical cure of the disease has indeed nicely demonstrated that the toxic excitant of the morbid process has its origin in the gland itself, but brings no proof that the varying degree of hypertrophy and hyperplasia is the cause of the disease. Surgical experience has, on the contrary, made it clear that the pathogenic processes do not necessarily depend upon the presence of an intact, hyperplastic and supposedly hyperfunctional gland, for in certain obstinate cases the symptoms may not subside so long as the tiniest rest of the toxic gland is allowed to remain. This not uncommon observation is excellent evidence that an intensive metabolic disturbance in the thyroid is at fault rather than a simple hyperfunction which would necessitate the presence of a large mass of thyroid tissue in order to produce the disease.

Clinical Evidence The relation of the iodine content to the degree of hyperplasia is of interest in this regard. As iodine is organically combined in the thyroxin molecule the amount of iodine present in the gland can be properly considered a certain gauge of its metabolic activity, duly recognizing, however, that such determinations cannot comprehend the amounts of iodine secreted in molecular association in thyroxin. It has been found that hypofunctioning goiters accompanied by cretinism are

markedly deficient in the iodine content. According to the hyperthyroidism theory one may then expect to find more rather than less iodine in thyrotoxic thyroids. Actually, Koehler (17) has noted as little as 1/30 of the normal amount present, Wilson and Kendall (18) from 1/50 to 1/20 of the normal. According to Marine and Lenhart's (19) studies, the iodine content of exophthalmic goiters varies inversely with the amount of hyperplasia present and shows in this regard no departure from the behaviour of the iodine content in various other thyroid conditions, normal and abnormal. Thus hyperplasia is known to decrease in non-toxic thyroid adenomata on exhibition of iodine or thyroid substance and iodine is stored in the gland. Precisely the same behaviour was observed by Koehler and Marine and Lenhart on administration of iodine and thyroid preparations to exophthalmic goiter patients. From these observations, it is evident that no evidence from the behaviour of the iodine content in exophthalmic goiter can be adduced in favor of the hyperthyroid theory.

Experimental "Hyperthyroidism" The similarity of the symptoms following the ingestion of thyroid material in excess of that of Graves' disease, also the well known aggravation of the disease by thyroid medication, constitute a further support of the hyperthyroidism theory. These statements are substantiated by experimental and clinical data which will now be analyzed.

From the experimental side, Klose (19) and Lampe, Liesegang and Klose (20) have reported the production of exophthalmic goiter symptoms, i. e., elevation of temperature, tachycardia, glycosuria, increased nervous irritability and, rarely, exophthalmos by feeding exophthalmic extracts to certain strains of fox terriers. These are among the very few experiments known to the writer in which exophthalmos, a cardinal symptom of human Graves' disease has been produced. Ballet and Enriquez (21), Baruch (22) and Klaus and Friedenthal (23) likewise report the production of exophthalmos by feeding thyroid preparations. Such results, however, merely demonstrate that extracts from the *pathological* thyroids of Graves' disease patients can produce a similar condition in animals, but do not prove that Graves' disease can be produced in animals by feeding large amounts of thyroid tissue or the thyroid hormone, which must be demon-

strated to prove the hyperthyroid hypothesis Klose and his associates, however, failed to elicit the above symptomatology when extracts from normal thyroid glands were fed and they themselves interpreted their results as supporting the dysthyroidism theory

A large number of workers have administered various iodine and thyroid extracts, also divers preparations from normal, goitrous, or thyrotoxic individuals without the appearance of a clinical syndrome capable of being designated as exophthalmic goiters. Among these may be mentioned Cunningham (24), Soupault (25), Hutchison (26), Gley and Claret (27), Gley (28) (who repeated Klose's work), Schoenborn (29), Fonio (30), Carlson, Rooks and McKie (31), Marine and Williams (32) Kendall (33) in injecting goats and dogs with large amounts of the isolated thyroid hormone gave the hyperthyroidism theory a severe test, but failed to observe the development of Graves' disease. This author states, "The general picture could not be differentiated from parathyroid tetany, idiopathic tetany or from certain phases of epilepsy." Though tachycardia and hyperpyrexia were produced, no exophthalmos was noted.

Summarizing then these data on the experimental causation of Graves' disease in animals, one must admit that the weight of evidence is against acceptance of the reproduction of this disease experimentally through use of thyroid preparations, including the thyroid hormone in chemically pure form.

DISCUSSION OF THE CLINICAL EVIDENCE IN FAVOR OF THE HYPERTHYROIDISM THEORY

From this side is reported the well known case of Notthafft (34) whose patient ingested 1,000 thyroid gland tablets within 5 weeks. There followed the development of the complete picture of exophthalmic goiter which gradually subsided when the thyroid medication was stopped. Several other similar cases have occurred in the literature. The writer has learned of still another by verbal communication of Professor Graham Lusk, New York.

It is, however, remarkable that, although over-dosage with thyroid preparations is of not uncommon occurrence the number of such cases has remained extremely few. These rare instances in which toxicity does occur, it would appear, might be accounted for by the previous existence of a latent tendency to

thyrotoxicosis, which, on the stimulation by the thyroid preparations, thereupon developed. Proof of the hyperthyroidism theory by such means would also necessitate the demonstration of an unquestionably normal thyroid gland in such instances. This is lacking and impracticable as well. It is also a well established clinical fact that most cases of exophthalmic goiter develop severer symptoms after the exhibition of thyroid preparations [Cerioli (35), Kocher (36), Goldflam (37), *et al*]. This aggravation of Graves' disease by thyroid medication can, however, only superficially be regarded as supporting the hyperthyroidism theory, for it is susceptible of other explanation. Thus the ingestion of large amounts of iodine and thyroxin may merely serve to provide a dysfunctioning gland with added material for the production of a toxic, imperfectly synthesized or anabolized thyroxin molecule, which may be the ultimate cause of the disease.

Finally, all experiments known to the writer on the experimental or clinical production of Graves' disease by thyroid preparations are subject to the same criticism, the question as to their interference with the normal thyroid metabolism with possible production of aberrant or pathological metabolites in the thyroid, which, themselves, cause the toxic symptoms. Convincing proof of the hyperthyroidism theory can only be brought by first excising the thyroid gland in experimental subjects and then producing *all* symptoms of the disease by introduction of large quantities of normal thyroid gland or, better, thyroxin. Such proof for the hyperthyroidism theory has not been forthcoming. One is here reminded of the inconsistency shown by the ready acceptance by many physicians of the experimental production of Graves' disease in animals on quite insufficient evidence, whereas the bacteriologist refuses to accept the bacterial cause of a given disease without its exact reproduction in animals or man.

The Contrast shown by the Symptoms and Signs of "Hyperthyroidism" and Hypothyroidism has been advanced in most text-books as a proof of the hyperthyroidism theory ever since the great emphasis put upon this apposition by Kocher. In regard to the value of the general clinical antithesis of these two conditions, McCarrison has shrewdly observed that the contrast shown by their symptomatology brings us no nearer the eluci-

dation of the *cause* of the morbid state of either. It seems to the present writer that it would be just as illogical to argue that acute mania is caused by "hyperfunction" of the higher cerebral centers because this form of insanity shows a diametric opposition, clinically, to acute melancholia. Such an argument would be regarded by every one as purely speculative.

Considered purely clinically, exophthalmic goiter presents a general picture of stimulation of the entire nervous system, a number of symptoms, viz, increased excretion of nitrogen and elevation of metabolism, the vagotonia, hyperpyrexia, nervous excitability, etc., differing only in degree from well known reactions of the organism to bacterial toxins, etc. On the other hand, the clinical picture of myxedema is one of widespread degeneration and consequent loss of function due to the loss of the anabolic action of the thyroxin on the tissues. The contrasting symptomatology of these two diseases is therefore most reasonably explained by a chemo-toxic effect in Graves' disease and loss of function in myxedema and cretinism, two essentially different pathological conditions producing, of course, differing symptoms.

Furthermore a critical survey of the *complete* symptomatology of both diseases renders it evident that the clinical antithesis of Graves' disease and hypothyroidism is largely confined to certain prominent symptoms as shown by the contrasting facial expression, mentality, the pulse rate and the like. In fact, a number of identical symptoms and metabolic phenomena are present in both conditions. Even Kocher admitted the common presence of edema, dryness and loss of hair and hair color, cutaneous dryness and pigmentation, and diminution of the salivary secretion. In addition to these there are other trophic and nutritional disturbances occurring in the two diseases but cloaked in the case of Graves' disease by the more striking evidences of general nervous excitation. To avoid repetition, reference can be made to the detailed consideration of the symptomatology from this standpoint developed in a later section.

Aside, however, from the identity of a number of the symptoms, a chief argument against acceptance of the hyperthyroidism theory has always remained the constant occurrence of a number of cases where clinically myxedema has been found accompanying Graves' disease. It is impossible to account for this condition on the hyperthyroid hypothesis. As Faure has em-

phasized, the conception of a thyroid gland in coincident state of hyper- and hypo-function is paradoxical. This fact alone would seem to the writer effectually to militate against the acceptance of the pure hyperfunctional theory.

Furthermore, myxedema is occasionally met with as a sequela of Graves' disease. Here may also be mentioned the not uncommon familial occurrence of Graves' disease and exophthalmic goiter. These facts would argue a common not a diametrically opposite, etiology.

Metabolism in Graves' disease and the Hyperthyroidism Theory. The increased metabolism in Graves' disease and the decreased metabolism in hypothyroidism is another argument used in favor of the hyperthyroidism theory. In order to apply certain criticisms to this argument it is necessary to analyze known metabolic data in thyroid disease.

During the past few years, since the general introduction of basal metabolic rate determinations in the study of thyroid disease, the contrast of thyrotoxicosis and myxedema has been further emphasized by the marked differences in the height of the gaseous metabolism in these two conditions. This metabolic antithesis has been particularly brought out by Plummer and Boothby, *et al*, of the Mayo Clinic in numerous articles which have served, on account of the large number of such metabolic studies reported and the prominence of their source further to strengthen the case of the "hyperthyroidism theory" among the medical profession at large.

The great assistance afforded the clinician by metabolic rate determinations in the diagnosis and treatment of thyroid disease has, however, led to overestimation of the importance of basal metabolism determinations in the diagnosis of these conditions. The influence of the thyroid as a regulator of oxygen consumption and of energy production has thus been thrust into the foreground without due consideration of the importance of thyroid function in cellular nutrition. Exception is here taken to the definition of the thyroid hormone advanced by Plummer and Boothby (38), influenced by Kendall's chemical viewpoint. They regard thyroxin as "a catalyst that accelerates the rate of formation of a quantum of potential energy in the cells of the organism." It is questionable whether this definition can be regarded at present as more than purely speculative, inasmuch as we re-

main in considerable ignorance of the exact chemical reactions involved in the formation of the "potential energy" in question. The frequent quotation, however, of this hypothesis in recent publications seems sufficient proof of the seriousness with which it has been generally received by the medical profession at large. This is due to the prominence of the source of this view. It would likewise indicate the desirability of authoritatively advancing only such new theoretical viewpoints as are completely defensible, both by critical analysis of the pertinent literature and adequate experimental support.

The chief function of the thyroid gland is the regeneration of old and growth of new cells by aiding in the synthesis of protoplasm. An attempt at a more specific definition seems inadvisable at present. Thus *anabolic* function is of vastly more importance than its *catabolic* effect, i. e., the production of heat and energy through combustive processes requiring oxygen. Both anabolism and catabolism, however, require oxygen consumption with liberation of heat, energy and carbon-dioxide. *The metabolic rate is very probably influenced by the thyroid, not directly for the purpose of control of energy and heat production, but only to the extent that these processes are necessary in the chemical reactions leading to the accumulation of intermediary metabolites and their synthesis into old or new protoplasm by the aid of the thyroid hormone.*

This view of thyroid function, which should indeed be self-evident from the marked influence that the thyroid is known to exert upon growth, was first emphasized by the present writer (39) in 1916, and developed in a later paper (40).

Even athyroid individuals are capable of considerable release of energy and heat production through other agencies, probably other ductless glands, which also function in the general nutritive processes of the cells. In cretinism and myxedema, even when there is complete absence of the thyroid gland, the gaseous exchange is decreased at most to 40 or 50 per cent, so at least 50 to 60 per cent of the normal metabolism must be accounted for otherwise than by activity of the thyroid gland. It will also be remembered that the heat centers in the medulla are still functioning even in athyreosis, as evinced by their response with pyrexia when sufficiently stimulated by bacterial toxins.

It is indeed probable that the decrease in the basal metabolism in hypothyroidism is to some extent *a compensatory retardation of the chemical processes of the cells of the body, whose exhaustion and disappearance would be hastened, in absence of a normal thyroid, by normal metabolic processes*. This seems indeed probable by the observed drop in the metabolic rate in cases of inanition with intact thyroids to levels as low as those seen in severe cases of cretinism and myxedema. That the lowered metabolism in hypothyroidism is due at least in part to "hormone starvation" is suggested by the gradual fall of the basal metabolism after complete removal of the thyroid, though it is capable of other explanation.

In view, then, of this conception of the metabolism of hypothyroidism, the decrease of the basal metabolic rate in hypothyroidism is regarded as a measure of an accompanying metabolic phenomenon rather than indicative of failure of a fundamental thyroid function.

The conception of the increased metabolism in thyrotoxicosis as being due simply to increased energy production, through increased thyroxin production, i. e., "hyperfunction" and "hyperthyroidism," is likewise subject to considerable criticism. Although a general indication of the severity of the disease, it has not proved possible to demonstrate an exact parallelism between the amount of "hyperfunctioning," thyroid parenchyma and the degree of elevation of the metabolic rate. Every internist of experience has observed cases of thyrotoxicosis still presenting considerably increased metabolic rates (for example, an increase of even 50 per cent) in individuals who possess but one-tenth or less of a toxic goiter largely removed through operation. Indeed, it is far more logical to explain the elevated metabolism in Graves' disease as a result of a general intoxication from abnormal products of thyroid activity. This reaction differs chiefly in degree from that produced by bacterial and other toxins in fevers, as has been stated. With regard to the increase in the metabolic rate observed after administration of large amounts of pure thyroxin, this observation fails to bring proof that the augmented gaseous exchange is not likewise due to a toxic stimulation, from the development of toxic intermediate products in course of the catabolism of amounts of thyroid hormone introduced experimentally in excess of requirements.

It by no means necessarily follows that the results ensuing after an ingestion of abnormal amounts of thyroid substance influence the basal metabolism *by the same means* in which it is held to the normal level by a normally functioning thyroid. Indeed, the very presence of a number of peculiar nervous and other symptoms in experimental hyperthyroidism would suggest a probable change in composition of the thyroid hormone responsible for the same. The long latent period reported by Kendall (41), as well as Janney and Isaacson (42) following the administration of a toxic dose of thyroxin can be considered as evidence in favor of some chemical transformation being necessary *before* the toxic outbreak with elevation of the metabolic rate can take place. Otherwise, one would expect an *immediate* rise of the basal metabolic rate which under normal conditions is one of the most labile of natural phenomena.

The Protein Metabolism The known facts concerning other aspects of the metabolism of hypothyroidism as contrasted with Graves' disease do not bear out the suggestion made by the behavior of the gaseous exchange, namely, that the one process is antipodal to the other,—“hypofunction” versus “hyperfunction.” Although the nitrogen metabolism is generally decreased in the former and increased in the latter condition, still the writer's experiments (40) have made it probable that the decrease of nitrogen output in cretinism is due rather to decreased protein absorption secondary to a decreased ability to retain synthetically nitrogenous metabolites in the body, possibly also to nitrogen “sparing.” In thyrotoxicosis the increased nitrogen output is best explained as a toxic loss of protein and nitrogen. It may also be noted that Janney (40), as well as Halvarsen, Bergeim and Hawk (43), found it possible to obtain an increased nitrogen balance by administering thyroxin to Graves' disease patients, a procedure which, according to the hyperthyroidism theory, should always have the opposite effect.

Creatinuria is frequently present in both Graves' disease and myxedema. Although *hyperglycemia* is the rule in the former and *hypoglycemia* in the latter condition, there is little regularity in this. Speaking generally, the most we can state is that irregularity in the carbohydrate metabolism is present in both diseases. In view of these discrepancies, it is impossible longer to accept that contrast shown by the metabolism of thyro-

toxicosis and hypothyroidism is conclusive evidence of the validity of the hyperthyroidism theory

Summarizing then the foregoing data, criticising the value of the contrasting behavior of the metabolism in hypothyroidism and thyrotoxicosis as a support of the hyperthyroidism theory, the following may be said

1 As the chief function of the thyroid is the generation and regeneration of the tissues by action of thyroxin on protein metabolites, not that of a mere catalyzer for the combusive processes, the basal metabolism, however significant clinically, is not of fundamental importance in the theory of thyroid disease

2 The lowered basal metabolism of hypothyroidism and the elevated metabolism of thyrotoxicosis are subject to other explanation than that of increased or decreased heat and energy production due to a simple kinetic hypothesis. The lowered metabolism of hypothyroidism may be caused at least in part by a compensatory retardation of metabolic processes in the cells to offset the decrease in amount of thyroxin, a hormone necessary for growth and repair of the cells and tissues. The increased gaseous exchange in thyrotoxicosis can be more reasonably explained by a toxic stimulation of the nervous and other tissues than by the effects of simple over-accumulation of the normally non-toxic synthetic hormone, thyroxin

3 The characteristics shown by protein, creatin and carbohydrate metabolism in exophthalmic goiter and hypothyroidism are not such as can be satisfactorily explained by the hyperthyroidism hypothesis

Summary of Criticisms of the Hyperthyroid Theory In the preceding pages the chief data and arguments in favor of the "hyperthyroidism theory" have been analyzed and reviewed in the light of modern knowledge. Sufficient evidence, it is believed, has been advanced to show that this time honored theory is supported by superficial and, in part, conflicting arguments, which constitute but a fallacious explanation of the etiologic, pathologic, metabolic and clinical data of Graves' disease

(To be continued)

EXPERIENCES IN TESTICLE TRANSPLANTATION

H LYONS HUNT, M D , L R C S , Edin

NEW YORK

I believe these cases are more often referred to the plastic surgeon than to the general or genito-urinary operators

The writer has had three cases referred to him during the past twelve months. That insufficient time since operation has elapsed, in the two which were operated on, is not questioned, as far as feeling in a position to state a definite result. I am reporting the cases, stating facts, as they were before operation and as they are now. I make no prognoses.

The first case, Mr. E. W. K., aged sixty, following a sudden mental shock in 1919, became completely impotent for a period of three months. He recovered to such an extent that he was able to get a partial erection after the administration of strychnine and a glandular extract. This period of ability to have a partial erection lasted until March, 1920, when he suffered a second mental shock to be followed again by the return of complete impotence. This second attack of impotence was associated with considerable debility, weakness in the lower extremities and insomnia. Glandular extracts and aphrodisiacs produced no beneficial result.

On June 29th, 1921, through the courtesy of the laboratories of Armour and Company, I secured a fresh testicle of a ram sent to my office in a refrigerated state. I refrigerated this gland in boric acid solution for thirty hours more and then making a longitudinal section 1 cm. in thickness, transplanted it into the patient's abdominal wall. The course of events in this case were as follows. Two days after operation the patient stated that he had enjoyed the first perfect night's sleep he had had in seven months and on awakening felt refreshed from his sleep, something he had not done before his insomnia began. Seven days afterward the center of the transplanted tissue began to become necrotic and an exudate began. Nine days after the patient began to have erections in the mornings. By the twentieth day the entire center of the transplanted gland had sloughed away, the wound had closed and the periphery of the gland could be

distinctly felt Normal sexual life, an increased appetite and a general feeling of well being now ensued The patient attributed all his general improvement to the operation At the end of six months he reported a gain of fifteen pounds in weight Last month (May, 1922) the patient called to request a reduction of his bill on the ground that he had changed his mind about the benefits received from the operation that since receiving the bill and thinking matters over he felt that his entire improvement or at least the greater part of it was psychological so there you are!

The second case, J P R, referred to me by Doctor F Mitchell of Sailors' Snug Harbour Hospital, Staten Island N Y, gave the following history Age 65, white, occupation, retired infirm sailor, state, bachelor For seven years had been suffering with the general symptoms of debility For the previous six months he had required assistance in ambulating, using two canes or a cane and crutch He had been unable to have copulation for months (six) due to lack of erections Weight, 140 pounds

Through the courtesy of the same laboratory, I secured a testicle of a freshly killed ram and within the hour transplanted a section similar to that used in case No 1, using the same general technic except the refrigeration The reaction was marked. Within forty hours the patient was confined to his bed, the abdomen was swollen and tympanitic, the temperature and pulse rose and the patient was genuinely sick Sloughing began on the seventh day and lasted three weeks At the end of this time he had recovered sufficiently to come to my office He had discarded his canes or crutch and cane (The operation was performed October 13th, 1921, his visit to my office, Nov 8th, 1921) I have seen this patient many times since operation In January his hair, which had been gray, began to become brown and at the present time he shows but a scattering of gray hair He states that he awakens daily with an erection and can copulate at will Very little of the original gland can be palpated This patient's general appearance, movements and cerebration have so markedly improved that it seems that only a biased mentality could think of denying the beneficial effects of the testicular gland

The third case mentioned, referred by Drs Williams and

Becket of the same institution in which case No 2 was a patient, is a man of 48 years of age who became blind and impotent simultaneously while in Government service in the Philippines ten years ago. This case is so recent (having been operated on only during the present month) that it is of no clinical interest at present and only mentioned on account of the peculiar coincident blindness and impotence.

Addendum—Aug 15, 1922. Potency was recovered in this case three weeks following operation.

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Book Reviews

THE ORGANS OF INTERNAL SECRETION, THEIR DISEASES AND THERAPEUTIC APPLICATION Ivo Geikie Cobb, M D, M R C S 3 ed
New York, 1921 Wm Wood & Company 352 p

A review of a previous edition of this work was published in this journal, 1917, 1, 469 The present edition does not vary greatly from that previously reviewed As indicated in the title, the book is an attempt to place at the easy disposal of clinicians those data of endocrinology that are of direct practical use An attempt is made to rationalize the data presented by placing them upon an alleged physiological foundation In this attempt the writer has been rather more successful than authors of other similar books in that for his physiology he has turned mostly to capable physiologists He has not, however, entirely escaped the pitfall into which authors of this sort of books are prone to fall, namely, to quote as authoritative the physiological conclusions reached by known bunglers or unheard of amateur investigators

The book is out of date in the assumption made that the function of the adrenal glands is determined essentially by their output of adrenin The author is distinctly more hospitable to alleged efficacy of various glandular products in everyday therapy than an unprejudiced study of the literature on organotherapy justifies The book concludes with a brief bibliography, the citations of which include some of the best and some of the poorest literature which has been published in the field covered

Anyone desiring that impossible entity, a brief and easy introduction to endocrinology, will find himself less likely to be misled by this than by most other books along this line—R G H

STUDIES IN DEFICIENCY DISEASES Robert McCarrison Oxford
University Press, N Y & Lond, 1921 270 p

This book on a very timely subject is based upon the investigations of the author in addition to the correlation of already existing facts The objects of the study were "to find out how the body goes sick in consequence of deficient and ill balanced food" and to deduce therefrom what forms of sickness in the human subject may reasonably be attributed to, or connected in their origin with, such foods McCarrison feels that the health of the gastro-intestinal tract is dependent on the adequate provision of accessory food factors A state of ill health of this

tract may be a prescorbutic manifestation of disease due to insufficient vitamin intake, especially when there is excess of fat or starch or both in the food

He thinks that vitamins in their action resemble hormones whose function is to stimulate metabolism. Disturbances of metabolism are bound up and in considerable measure are dependent on the disturbance of endocrine function which results from the same cause. It seems that both the functional perfection and correlation of the endocrine organs are dependent upon a properly balanced and vitamin-containing food supply. Dietetic deficiency means endocrine insufficiency.

Effects of food deficiency on the organs of internal secretion are shown by atrophy of the thymus, spleen, testicles, ovary, thyroid and parathyroid and by hypertrophy of the adrenals and pituitary. This hypertrophy may perhaps be compensatory. An adequate supply of vitamins is essential to perfect nutrition of the heart and kidneys.

The book is a valuable addition to the literature on the vitamins and deficiency diseases, especially in relation to the endocrine system.—M B G

DAS HYPOPHYSENGEWICHT BEIM MANNE UND SEINE BEZIEHUNGEN. Dr. Paul Petersilie, Langensalza, 1920. Verlag von Wendt & Klauwell, 26 p.

The author examined the hypophyses of 189 men who died during the war. The average weight was found to be 620 mg, the lowest 300 mg and the highest 900 mg. There was found no relation between its weight and the locality in which the person lived. The data indicate that up to the 30th year the weight increases, then remains unaltered until the 40th year, when it gradually diminishes. Small persons generally have a small hypophysis and tall persons have a larger one. Usually the greater the weight of the gland, the greater the compactness of the bone structure. Thus there seems to exist a relation between the length of the body and the weight of the gland, but not between the weight of the body and the weight of the gland. When geographical influences are eliminated we may say that a heavy hypophysis is accompanied by a light *thyroid* and vice versa. When the hypophysis is heavy, the *testicles*, *pancreas* and kidneys are also heavy. No relation exists between the weight of the hypophysis and the *adrenals*.—J K

EIN FALL VON BEIDERSEITIGER HODENOERDOPPELUNG (A CASE OF FOUR TESTICLES). Dr. P. Kern, Langensalza, 1921. Verlag von Wendt & Klauwell, 19 p.

In this small brochure a good description has been given of a man with four testicles, hypospadias penis and spina bifida.

occulta The patient is still living Sexual desires were normal, not exaggerated The spermatozoa were larger than normal This is the sixth case reported (See Day, *Endocrin*, 3, 95)—J K

DIE ERFOLGE DER STEINACHBEHANDLUNG BEIM MENSCHEN Dr L Lenz and Dr P Schmidt, Berlin, 1921 Verlag von G Tietzen, 32 p

A popular little book, written without critical acumen The authors believe rejuvenation to be absolutely certain Operation is also advised for fatigue, palpitations, giddiness and headache The publication of this type of popular medical literature is deplorable—J K

ENDOCRINOLOGIA Livini, Rondoni, Peppere, Pende & Coronedi, Milano, Italy, 1922 Istituto Sieroterapico Milanese, 350 p

The volume comprises a group of lectures on endocrinology given to newly graduated doctors The anatomy and embryology, physiopathology, anatomo-pathology, the relations of the endocrine glands to nervous and mental pathology and the therapeutic applications are discussed in a clear and concise way and great care is taken by each of these professors not to overindulge in personal views The object of this book and the steady warning given to young practitioners not to be misled by untimely enthusiasm are especially worthy of praise
—G V

LES GLANDES SURRENALES ET L'HYPOPHYSE Dr R Porak, Paris, 1922 Librairie Octave Doin, 103 p, 8°

This work includes three distinct studies the first, of Addison's disease, the second, of the therapeutic action of pituitary extracts, and the third, upon adrenal insufficiency, but a common purpose reigns throughout the study, that of physiological pathology "Today," says the author, p 67, "where clinicians abuse their diagnosis of adrenal insufficiency, it is well to recall experimental labors and through their light to criticize clinical observations" It is in this critical spirit that the author examines the question studied And this criticism, both wise and prudent, is due to the fact that he always refers to the teachings of physiological pathology, hence his description of the data bearing upon acute adrenal insufficiency slow insufficiency, and the bearing of these upon adrenal insufficiency in the clinic of human diseases, its rapid and subacute forms In all cases the gravity of the disease does not appear at all connected with the diminution of adrenalin in the pathological adrenals Adrenal insufficiency, in fact, appears as such only in the clinic, and the

treatment by means of adrenalin has never in reality ameliorated these morbid conditions any more than it has ameliorated Addison's disease. Thus, in the same spirit, Porak discusses pituitary opotherapy, showing that no absolute conclusion may be drawn from the numerous cases in which it has been used, and showing particularly that even if we are familiar with the pharmacologic effects of these extracts, their biological meaning has entirely escaped us—E G

GHIANDOLE A SECREZIONE INTERNA A Peppere Vol 8 in Trattato di Anatomia Patologica, Pio Foà Torino, 1922 Unione Tipografica Editrice Torinese 300 p, 8°

The subject is exhaustively treated with objective views inspired by thoroughly scientific criticism. The vast bibliography shows that none of the foreign publications has been overlooked and may prove of some interest by bringing the rich scientific contribution on the part of the Italian scientists to the notice of the readers. The widely known name of Prof P Foà is in itself a guarantee of the exceptional value of this work. The first volume, on Blood and Hematopoietic Organs, by Prof Foà, has, in less than six months, reached its second edition —G V

THE FOLIA ANATOMICA JAPONICA Vol 1, No 1, March, 1922

A new journal devoted to the publication of original material of anatomical research, macroscopic and microscopic anatomy, embryology, experimental morphology, physical anthropology, macroscopic and microscopic methods of investigation, etc. Under the management of K Okajima, Keio University, Tokyo—R G H

ARCHIVES OF OCCUPATIONAL THERAPY The official organ of the American Occupational Therapy Association Vol 1, No 1 Feb, 1922

A new journal devoted to the publication of the fundamental data which are now scattered in many periodicals or which now lack the proper means of dissemination. It will be of interest to not only the medical and surgical world, but also to those interested in social service, to the psychologist, to business organizations interested in the educational recreational value of occupational therapy, etc. Edited by Wm R Dunton, Jr, M D. Published bimonthly by Williams & Wilkins Company, Baltimore, Md—R G H

Abstract Department

(ADRENIN THYROID) The physiological action of the proteinogenous amines V Vegetative nervous system and metabolism (Beitrage zur Kenntniss der physiologischen Wirkung der proteinogenen Amine V Vegetatives Nervensystem und Stoffwechsel) Abelin (J), Biochem Ztschr (Berl), 1922, 129, 1-49

A study of the action of adrenalin, tyramine, phenyl-ethylamine, tyramine thyroid substance, cholin, acetylcholin, histamine, pilocarpin and atropin on the gas exchange of the white rat, and the effect of tyramine and phenylethylamine on the gas exchange of a thyroidectomized dog All the compounds with the exception of histamine and acetylcholine increased the gas metabolism and frequently produced diuresis Glycogen mobilization, hyperglycemia and glucosuria occurred Tyramine and phenylethylamine are additive in their action on metabolism, for when sub-effective doses of either are administered together with sub-effective doses of thyroid substance there is produced a marked increase in gas exchange These observations make it appear probable that the action of the thyroid on metabolism is only an expression of a generalized influence on the vegetative nervous system and that this is of great significance in the regulation of the kind and degree of total metabolism The dose and the method of administration are important factors, for smaller doses are effective when the compounds are given per oram Histamine has no effect on the gas exchange, while acetylcholin produced a significant reduction —F S H

(ADRENIN) Treatment of sciatica (Behandeling van ischias) Adels (M H J), Vox med (Utrecht), 1922, 22, 82-83

In very rebellious cases of sciatica the author recommends the injection of 20 mg of novocain and 1 mg of adrenalin into the nerve —J K

Very severe paroxysmal adynamia with ADRENAL insufficiency (Paroxysmale schwerste Adynamie bei Insuffizienz der Nebennieren) Bauer, München med Wehnschr, 1922, 69, 797, Klin Wehnschr (Berl), 1922, 1, 1281

Adynamia may be the only symptom of insufficiency of the adrenals The author observed, for example, a patient who had attacks of weakness, lasting for \pm 2 hours, during which he was not able to stand In one case an amyloid degeneration of the cortex was found, but no important changes in the medulla —J K

(ADRENIN PITUITRIN) Studies on the visceral sensory nervous system XII The response of the isolated oesophagus of the frog and the turtle to certain drugs Bercovitz (E), Am J Physiol (Balt), 1922, 60, 219-233

Carlson and Luckhardt have reported that stimulation of the peripheral vagus in the turtle causes inhibition of the circular neuromuscular mechanism of the oesophagus in its upper two-thirds, and contraction of the longitudinal system in the region of the cardia. The present paper reports the results of an attempt to throw further light on this subject by the use of a number of so-called neurotropic and myotropic drugs. Among these were adrenalin and pituitrin. In the frog's oesophagus adrenalin caused a uniform inhibition of the longitudinal system. In 66% the circular system was stimulated, in 33% it was inhibited. Armour's pituitary liquid caused uniform inhibition of the circular and longitudinal systems. In the turtle adrenalin caused a profound and lasting stimulation preceded by temporary inhibition.—T C B

(ADRENIN) How the blood calcium is changed by drugs (Der Calcium spiegel im Blute und seine Beeinflussung durch verschiedene Gifte) Billigheimer (E), Klin Wchnschr (Berl), 1922, 1, 256-258

In 15 patients adrenalin 13 times caused a temporary decrease of the amount of calcium in the blood. The decrease was most marked in patients in whom the change in pulse, blood sugar and blood pressure was most marked also.—J K

The effect of ADRENALIN on healthy persons Bjure (A) & Svensson (Y), Upsala Läkaref Forh, 1921, 26, 1-23, J Aug Hammar, Festskrift Each article is pagged separately

The authors, at intervals of a month, injected epinephrin into five healthy medical students, once in a dose of 0.5 mg and twice of 1 mg. A great many clinical examinations were made with the following results. The effects of epinephrin injections vary considerably in different healthy persons and in the same person at different times. There was always found a rise of the content of blood sugar with a maximum in about three-quarters hour and a lymphocytosis with the maximum of about one-half hour after the injection. Frequently a rise of the blood pressure and the pulse rate with the maximum one-half hour after the injection was observed. The red blood corpuscles showed in one experiment an evident rise persisting at least 3 hours. The quantity of urine and the absolute quantity of NaCl in the urine were often increased. Sometimes, however, the urine and the NaCl were decreased. No definite changes were noted in the respiration rate, the percentage of NaCl in the blood or the haemoglobin.—H B

Intracardial injection of ADRENIN in an infant (Intrakardiale Adrenalinjektion bei einem vier Monate alten Säugling) Blüedung, Klin Wchnschr (Berl), 1922, 1, 196, München med Wchnschr, 69, 309-310

In a child of 4 months 0.2 cc of a 1% solution of adrenin was injected into the heart, which had discontinued beating during narcosis. There was complete recovery.—J K

Developmental disturbances and arrests of the ADRENAL in Addison's disease (Entwicklungsstörung und Entwicklungshemmung der Nebennieren bei Addison'scher Erkrankung) Bloch (R), Beitr z path Anat u z allg Path (Jena), 1920, 67, 71-113

Processes resembling disturbed or arrested development of the adrenal are to be observed in certain cases of Addison's disease. The author finds the medulla enlarged and the cortex lacking or degenerated.—W J A

The analgesic action of ADRENIN in certain forms of ophthalmic neuralgia (L'action analgésique de l'adrénaline dans certaines formes de névralgie ophthalmique) Bonnefou, Compt rend Soc de biol (Paris), 1922, 86, 374-376

In cases of neuralgia of the ophthalmic connected with an infectious condition in which the painful crisis is preceded by a vasomotor aura, the instillation into the conjunctival sac of a few drops of adrenalin, 1:1000, may avert the crisis. If the instillation is too tardy, after lachrymation, photophobia and periocular injection has set in, the adrenalin does not avert the crisis, but notably shortens its duration. If given during a neuralgic attack its effect is nearly null. A case is cited.—T C B

Acetonuria and glycemia after injection of ADRENIN in dysentery (Azetonurie und experimentelle Adrenalinglykämie bei Ruhr) Buttenweiser, München med Wchnschr, 1922, 69, 83

In 2 patients with acetonuria in whom adrenalin was injected there was no hyperglycemia and in 5 others it was seen in a very light degree. When 100 gms of glycose was given before the injection of adrenalin, hyperglycemia became much more marked.—J K

(ADRENIN) On the automatic movements of the isolated iris Cate (J T), Versl d k Akad v Wetensch Wis-en natuurk Afd (Amst), 1921, 30, 143-144

By employing a method for magnifying contractions of iris muscle 16 times, the author found that a supply of oxygen causes a lasting contraction of the muscle, but a diminution in rhythmic movements. Pilocarpine hastens the movements, adrenaline slows them. Pilocarpine and choline both increase the strength of the contractions, while adrenaline weakens and atropine stops them.

—Physiol Abst, 7, 17

Rôle of the vegetative system in the production of hypertonia of voluntary muscles I Action of ADRENIN and of calcium chloride II Action of eserin and of atropin III Action of ADRENIN, eserin and atropin in successive injections IV Rôle of the sympathetic and parasympathetic respectively Idea of amphotonia (Rôle du système végétatif dans le production de l'hypertonie des muscles volontaires I Action de l'adrénaline et du chlorure de calcium II Action de l'ésérine et de l'atropine III Action de l'adrénaline, de l'ésérine et de l'atropine, employées en injections successives IV Rôle respectif du sympathique et du parasympathique Notion de l'amphotonie) Daniélopou (D), Radović (A) & Carniol (A), *Compt rend Soc de biol (Paris)*, 1922, 80, 625-634

A series of four papers dealing with tonus of striped muscle Of endocrine interest in that adrenalin was one of the substances used to show the innervation of voluntary muscle by the autonomic system—T C B

(ADRENAL) The influence of x-rays on the endocrine glands (Beeinflussung endokriner Drüsen durch Röntgenstrahlen) David, München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1281

Animal adrenals were directly exposed to x-rays (the organs were exposed by an operation) Sometimes the adrenalin content was increased, sometimes lowered This problem should be studied by application of known quantities of x-rays to the naked organs of internal secretion—J K

(ADRENAL) Addison's disease with pluriglandular insufficiency (Addison'sche Krankheit mit pluriglandularer Insuffizienz) Deusche, München med Wchnschr, 1922, 69, 373

A man of 43 with Addison's disease showed the following symptoms very low blood pressure, pigmentation, asthenia, cachexia, thin hair and beard, dry atrophic skin, no sexual desires, small thyroid, normal testicles and hypophysis (as far as may be judged by clinical examination), and pernicious anemia—J K

(ADRENAL) Morbus Addison Fahr, Klin Wchnschr (Berl), 1922, 1, 501, München med Wchnschr, 1922, 69, 227, Deutsche med Wchnschr (Berl), 1922, 48, 613

A woman of 53 had bronzed skin, normal blood pressure and cachexia At autopsy it was found that the adrenals weighed 1 and 0.5 gm, the medulla was normal, the cortex, atrophic—J K

Is extirpation of an ADRENAL in epilepsy justified (Kritisches zum Artikel Specht's Is die Nebennierenextirpation bei Epilepsie berechtigt)? Fischer (H), Zentralbl f Chir (Leipz), 1922, 49, 113-115

Fischer found that after removing an adrenal it was not possible to produce spasms in an animal by amyl nitrite, but Specht could not confirm this. Specht made the mistake of administering pure amyl nitrite without air, causing the animal to suffocate and get spasms with or without adrenals —J K

(ADRENALS) Experimental studies on spasms (Tierexperimentelle Krampfstudien) Fischer (J), Zentralbl f Chir (Leipz), 1922, 49, 591-595

H Fischer has reported experiments showing that ablation of one adrenal is followed by a lowered sensibility for spasmodic poisons and toxins. His work has not been confirmed by Specht, whose experiments have been abstracted in Endocrinology. J Fischer now states that Specht has never properly read the publications of H Fischer. Specht seems to believe that all spasms are identical—that there is no difference between epilepsy and other spasms. Ablation of an adrenal is an operation without risk and as cases have been described in which this operation has been performed with some success and as there is no other treatment, it should be tried in epilepsy. Specht's experiments with amyl nitrite have been carried out with poor technique. In many experiments the animals did not inhale amyl nitrite, but nearly suffocated because the mask was too small. The use of fresh amyl nitrite is of great importance. To test the sensibility of an animal after ablation of an adrenal, it is necessary to wait until the animal is quite recovered from the shock of operation and narcosis. When all these precautions are taken the animals show a lowered sensibility after ablation of an adrenal. Before the ablation the animals often lose consciousness, when amyl nitrite is administered after the ablation this is rare. When 0.2 mg of adrenalin per kg body weight or 0.2 mg of hypophysis per kg body weight was injected into a normal rabbit 10 minutes before the inhalation of amyl nitrite, spasms were much more intense, causing many of the animals to die —J K

The function of the ADRENALS IV The rôle of the ADRENALS in the vasomotor phenomena of asphyxia. Purely nervous mechanism of these phenomena (La fonction des surrénales IV Du rôle des surrénales dans les phénomènes vaso-moteurs de l'asphyxie Mécanisme purement nerveux de ces phénomènes) Gley (E) & Quinquaud (A), Arch internat de physiol (Liège & Par), 1921, 18, 22-34, abst, Physiol Abst, 7, 51

In dogs whose bulbo-medullary axis has been completely destroyed there is no indication of the well known cardiovascular reaction of asphyxia and no modification of arterial pressure. However, the vessels in this condition remain sensible to the excitant which acts directly on their musculature to the direct excitation of the different nerves as to different poisons—to adrenalin in particu-

lar After division of the two large splanchnics, an operation which renders all secretion of adrenalin impossible, the vasomotor reaction of asphyxia is not modified After double adrenal ablation the same is true Vasomotor reactions are not, then, event partially of humoral origin (under the influence of adrenal secretion), they are of central nervous origin —R G H

Relation between the changes in the H-ion concentration in the vena porta and the hyperglycemia after ADRENIN administration (Ueber den Zusammenhang zwischen H-ionkonzentrationsverschiebung im Pfortaderblute und der Hyperglykämie nach Adrenalininjektion) Gottschalk (A), München med Wehnschr, 1922, 69, 797, Klin Wehnschr (Berl), 1922, 1, 1281

When the vena porta is ligated hyperglycemia occurs The author was able to prove that this was not due to a changed circulation in the liver (no details are given) When alkali is given the effect of adrenalin on the blood sugar is much less marked The respiration of the liver tissue is markedly diminished by injection of adrenalin Adrenalin thus acts directly upon the liver cells —J K

The relation of the ADRENALS to fatigue Hartman (F A), Waite (R H) & Powell (E F), Am J Physiol (Balt), 1922, 60, 255-269

See Endocrin, 6, 511-518 —T C B

Perfusion of the medulla of the terrapin (Pseudomys troostii) with ADRENALIN Heinekamp (W J R), J Pharmacol & Exper Therap (Balt), 1922, 19, 131-134

These experiments were carried out as a reply to Bush (see Endocrin, 5, 481) The author found that adrenalin, perfused through the medulla of Pseudomys troostii, causes partial or complete inhibition of the heart —F A H

ADRENAL extirpation and epilepsy (Nebenniercextirpation und Epilepsie) Heymann (E), Zentralbl f Chir (Leipz), 1922, 49, 255-257

Treats only the technique of the operation —J K

Tumor of the right ADRENAL (Tumor der rechten Nebenniere) Horner, Klin Wehnschr (Berl), 1922, 1, 707

A short note Hematuria was the only symptom manifested Death resulted from metastases in the lungs —J K

Energometric studies on the influence of ADRENIN on the circulation (Energometrische Untersuchungen über die Wirkung des Adrenalins auf den Kreislauf) Hotz (A), Deutsches Arch f klin Med (Leipz), 1922, 138, 257-269

In very detailed and exact experiments on healthy children the author studied the influence of adrenalin on the blood vessels. It has been proved in animals that injection of adrenalin is followed by a rise of the pulse volume of the peripheral arteries. The same was proved in case of the arteria brachialis of children, showing that the blood vessel becomes larger under the influence of adrenalin. The systolic blood pressure rises, the pressure of the wall of the vessel ("Wanddruck") rises also, but the diastolic pressure often sinks. This last fact is probably due to an increased flow of blood to the right heart. Cloetta and Anderes were able to prove in animals that when adrenalin is injected the size of the lungs is increased by this increased flow of blood to the right heart. Therefore, Hotz supposes that the same occurs in man and that this explains the diastolic blood pressure after the injection of adrenalin.—J K

A criticism on Specht's article "Is ADRENAL ablation in epilepsy justified?" (Kritische zu dem Artikel "Ist die Nebennieren-exstirpation bei Epilepsie berechtigt?") Kersten (H), Zentralbl f Chir (Leipz), 1922, 49, 482-485

The author criticises Specht's article (Endocrinol, 1922, 6, 130). Both the form of the mask with which the amyl nitrite is given and the number of drops administered are highly important. It is necessary also that it be fresh, for old solution contains HNO_2 and ethyl valerate and are inactive. Normal rabbits, after ablation of an adrenal, have much less severe spasms when they inhale amyl nitrite than before this ablation. During pregnancy the adrenal system becomes hypertrophic and Kersten observed that his pregnant animals showed spasms sooner when this substance had been administered than did the normal controls. Hypertrophy of the adrenals is also seen after castration and in these cases, too, spasms after inhalation of amyl nitrite occur earlier than in normal animals. Kersten states that ablation of an adrenal causes a diminished sensitiveness to spasmodic substances and that hypertrophy of the adrenals is followed by an increased sensitiveness for such substances.—J K

The influence of ADRENIN on the excretion of uric acid (Die Ausscheidung der Harnsäure unter Einfluss von subkutanen Adrenalingaben) Krauss (E), München med Wchnschr, 1922, 69, 761

Though the blood contains much uric acid in primary hyper-tonia, the urine contains but little. When adrenalin is injected in healthy persons the excretion of nitrogen, urea, creatinin and NaCl is augmented, the excretion of uric acid is diminished as soon as the blood pressure rises. The excretion of water may be increased or diminished. When the blood pressure is high after the injection of adrenalin the serum contains large amounts of uric acid. The excretion of the uric acid seems to depend upon the blood pressure.—J K

The influence of veratrin and EPINEPHRIN on skeletal muscle
 Kruse (T K), J Pharmacol & Exper Therap (Balt), 1922, 19,
 266

Epinephrin did not produce veratrin-like effects on frog's skeletal muscle Solutions up to 0.01 per cent were employed —F A H

(PITUITRIN, EPINEPHRIN) Certain aspects of the part played by the liver in the regulation of the blood volume Lamson (P D), J Pharmacol & Exper Therap (Balt), 1922, 19, 267-268

If hemoglobin can be used as an index of the fluid content of the blood, epinephrin would increase the rate of fluid loss, largely due to its action in the liver Pituitrin would decrease the rate of fluid concentration from the circulation very greatly, holding fluid injected into the circulation for over three hours It also overcomes the action of epinephrin The increased rate of fluid loss after epinephrin has been accounted for by constriction of the hepatic veins and an increased filtration pressure in the liver —F A H

The influence of ADRENIN on the permeability of the sarcolemma
 (Über die Einwirkung des Adrenalins auf die Permeabilität von Muskelfasergrenzschichten) Lange (H), Klin Wchnschr (Berl), 1922, 1, 70

A short note Adrenalin diminishes the permeability of the tissues between the muscles fibres —J K

The action of ADRENIN on muscular excitability and fatigue (Action de l'adrénaline sur l'excitabilité musculaire et sur la fatigue)
 Lapicque (M) & Nattan-Larrier (M), Compt rend Soc de biol (Par), 1922, 86, 474-476

Experiments were made on the muscle and nerve of frogs, toads, crawfish, snails, frog's heart, etc The conclusion is that adrenalin diminishes the "chronaxie" of all the tissues considered, as well as the fatigue following repeated excitation —T C B

A hemorrhagic cyst of the ADRENAL cortex (Beitrag zur Kenntnis der Struma suprarenalis cystica haemorrhagica) Laxh (C H), Beitr z klin Chir (Tubing), 1922, 125, 467-475

A cystic tumor was removed from a woman of 31 It contained cholesterol and erythrocytes Cortex tissue of the adrenal was found in the wall Only 10 similar cases have been published

—J K

(ADRENIN) The action of some drugs on the vessels, studied with the capillary microscope (Mikrocapillarbeobachtungen über die Wirkung eingiger Gefaszmittel) Moog (O) & Ambrosius (W), Klin Wchnschr (Berl), 1922, 1, 944-947

Adrenalin causes a narrowing of the arteriolar and the capillaries. Only the arterial part of the capillaries shows a contraction. The blood stream becomes slower and the tissues get less blood. When the capillaries are studied with the skin microscope after the injection of adrenalin they have a granular aspect. Contraction of the capillaries occurs only when there is a blood stream in these capillaries. When, for example, the blood stream is temporarily arrested by tying a cord around a limb, adrenalin does not produce contraction. When the vessels are damaged by a want of oxygen or by a large quantity of carbonic acid the influence of adrenalin is much less intense. Adrenalin is not decomposed by the tissues as is proved by the fact that when injected into a limb tied by a cord, which, a few minutes later is taken away, the action of adrenalin is quite normal. In the same way, when adrenalin is injected and another limb is tied, it does not act on the vessels of that limb. If 10 to 20 minutes later the cord is taken away the action of the adrenalin on the arterioles may be seen by the skin microscope.—J K

Disturbed formation of adrenin in the ADRENALS due to external causes, and its biological significance (*Störungen der Adrenalinbildung in den Nebennieren unter äusseren Einflüssen und ihre biologische Bedeutung*) Peiser (B), *Klin Wchnschr (Berl)*, 1922, 1, 628-629

The author found the adrenaline content of 150 adrenals to be about 30% less than before the war. By experiments on guinea pigs he was able to prove that this was due to underfeeding.—J K

The vasoconstrictor action of ADRENIN and strychnine Plumier (L L), *Arch internat de physiol (Liège & Par)*, 1921, 18, 434-445

The author studied the action of these compounds by measuring simultaneously the pressure from the central end of a carotid artery and the peripheral end of the two crural arteries, after having sectioned the nerves of one of the paws. This method devised by Nolf (*Bull Acad roy de méd de Belg*, 1902, p 895) does not determine whether the vasoconstrictor substance acts on the neural centers or on the vessel walls. It was shown that strychnine apparently acts on the former and adrenalin on the latter, as was to be expected.

—Chem Abst

Changes in the H-ion concentration after injection of ADRENIN (*Änderungen in der Wasserstoffionenkonzentration nach Adrenalininjektion*) Pohle, *München med Wchnschr*, 1922, 69, 797, *Klin Wchnschr (Berl)*, 1922, 1, 1281

In both the vena porta and the vena hepatica the H-ion concentration was largely increased after injection of adrenalin. This increase was preceded by the rise of the blood sugar.—J K

The cardio-vascular action of ADRENIN in man Difference of physiological effect in the healthy and pathological states (*L'action cardio-vasculaire de l'adrénaline chez l'homme Différence de l'effet physiologique à l'état sain et à l'état pathologique*) Porak (R), J de physiol et de path gén (Par), 1920, 18, 1194-1202

In the normal subject the rise of blood pressure for a given dose varies according to the individual This fact must be taken into account in testing the reaction to adrenalin in disease Thus the indications of disorders of internal secretion may be modified by those due to infections of the vascular or nervous system

—Physiol Abst , 6, 72

On the mechanism of the ADRENAL function (*Sur le mécanisme de la fonction surrénale*) Rebello (S) & Pereira (M de M), Compt rend Soc de biol (Par), 1922, 86, 325-327

It has been shown that adrenalin when injected into the lower extremity of a frog, attached to the body only by the sciatic nerve, exerts its effect at a distance The following hypothesis is given Histologically and embryologically the suprarenal medulla must be considered an annex to the sympathetic, or as a part of that system differentiated for certain functions Adrenalin is easily oxydized Its existence in the blood beyond the vena cava inferior is uncertain It is difficult to admit a sympathicotonic effect by way of the arteries of a substance so sensitive to oxygen, and it seems simpler to admit that adrenalin, produced by the chromophil cells, exercises an exciting action on the nerve terminations, which is continuous, and is transported to a distance by maintaining the sympathetic tonus —T C B

Test for ADRENIN (*Über Adrenalin*) Russmann, Klin Wchnschr (Berl), 1922, 1, 654

A 4 cc slightly acid solution of adrenalin, 1 drop of saturated HgCl_2 solution, 3 drops of saturated sulfanilic acid and 1 cc of a solution of KIO_3 boiled together for 1 minute produces a brown color The reaction is positive with a solution of adrenalin of 1 50 million (The concentration of the KIO_3 is not given)—J K

Reply to Fischer's criticism on my article, "Is ADRENAL ablation justified in Epilepsy?" (*Erwiderung auf die Kritik Fischer's zu meinem Artikel "Ist die Nebennieren extirpation bei Epilepsie berechtigt?"*) Specht (O), Zentralbl f Chir (Leipz), 1922, 49, 402-403, Beitr z klin Chir (Tübing), 1922, 125, 347-367

Specht's original article has been abstracted in this Journal, 1922, 6, 130 Fischer has criticised Specht for giving amyl nitrite to his animals in such a way as nearly to suffocate them Later on, however, Specht used exactly Fischer's technique The results were the same in both cases Specht therefore persists in his previous conclusions —J K

On the relationship between the ADRENAL gland and the THYROID
 Scrimger (F A C), Canad M Ass J (Montreal), 1922, 12,
 316-317

The two recognized groups of goitre are cited, exophthalmic and the toxic adenoma. A third group is set up, similar to the exophthalmic in some respects but lacking the exophthalmos. Microscopically, areas are "indistinguishable from the generalized hyperplasia associated with true Graves' disease". It is suggested that, in this third group the thyroid and the adrenal or other ductless glands are diseased, while in the other groups the thyroid alone is diseased. Evidence is gleaned from the literature to prove the point.—J H

Complete ADRENAL insufficiency Soler (F L), Rev méd de Hamburgo, 1921, 2, 107-109

The conclusions are (1) Complete removal of the adrenals in dogs does not lead to a functional cessation of motility nor to an auto-curarisation. (2) The toxic results affect chiefly the brain cortex, giving rise to symptoms similar to those which can be induced hypnotically.—Ber ü d ges Physiol, 10, 97

The function of the ADRENAL cortex (Ueber die Funktion der Nebennierenrinde) Stephan (R), München med Wchnschr, 1922, 69, 339-342

Stephan examined a large number of women during, or a short time before, the onset of the menopause and nearly always found a marked hypertension and a slight polycythemia (5.8-7 millions of erythrocytes). The blood pressure and the number of erythrocytes do not run parallel. When the left adrenal in such women was exposed to intense x-rays, no influence was seen on the blood pressure, but the number of erythrocytes always decreased and stayed normal for about a week. The same was seen in hypertension with sclerosis of the kidneys. In a woman suffering from a cancer of the stomach the author exposed the left adrenal to the same amount of x-rays. Necropsy showed a necrosis of the cortex with a normal chromaffin tissue. The cortex seems to be radiosensitive, while the medulla does not. Therefore, it is probable that the number of erythrocytes has some relation to the cortex, as this number is diminished by the action of x-rays. It is an important question whether the polycythemia of the menopause is due to an increased formation or a diminished destruction of red blood cells. Stephan has been able to prove in other experiments that the amount of proteolytic enzymes in the blood runs parallel with the destruction of red cells. In the menopause these enzymes are diminished and, therefore, it is stated that the polycythemia is due to a diminished hemolysis. After x-ray treatment the proteolytic enzymes in the blood rose, hemolysis increased, and the number of red blood cells

decreased As this hemolysis is a function of the spleen it is stated that it is under the control of the adrenal cortex —J K

The action of drugs on the output of EPINEPHRIN from the ADRENALS VIII Morphine Stewart (G N) & Rogoff (J M), J Pharmacol & Exper Therap (Balt), 1922, 19, 59-85

Morphine, administered subcutaneously or intravenously caused in cats an increase in the rate of output of epinephrin, sometimes as much as ten times the initial rate These results were obtained in animals under the influence of ether or urethane The symptoms produced by morphine in non-anesthetised cats seem to be independent of the adrenals, for removal of one adrenal and part of the other and denervation of the remainder, does not appear to modify them Morphine caused little or no increase in the epinephrine output in dogs —F A H

The influence of muscular exercise on normal cats compared with cats deprived of the greater part of the ADRENALS, with special reference to body temperature, pulse and respiratory frequency Stewart (G N) & Rogoff (J M), J Pharmacol & Exper Therap (Balt), 1922, 19, 87-95

No difference in rectal temperature, pulse rate, respiratory rate, resistance to fatigue or recovery from fatigue, was observed in cats with one adrenal and a large part of the other removed or the second one denervated, as compared with normal cats, when subjected to prolonged muscular exercise After severe muscular exertion there is a definite although not great depletion of the epinephrin store in an adrenal with intact nerve supply, using a denervated adrenal as a control Considerable exertion, falling short of great fatigue may not cause depletion —F A H

The influence of morphine on normal cats and on cats deprived of the greater part of the ADRENALS, with special reference to body temperature, pulse and respiration frequency and blood sugar content Stewart (G N) & Rogoff (J M), J Pharmacol & Exper Therap (Balt), 1922, 19, 97-130

The marked hyperthermia caused by morphine in cats has been studied in connection with the development of the general symptoms, the changes in the pulse and respiratory frequency and the sugar content of the blood It has been observed that there is no close association between the hyperthermia and the hyperglycemia, or even the degree of muscular activity The hyperthermia and the general symptoms develop in the same way, and reach the same intensity in cats from which the greater portion of the adrenal tissue has been removed and the remaining fragment denervated, as in normal cats An increase in blood sugar was observed after asphyxia, provided there was a storage of glycogen Morphine did

not cause an increase in blood sugar in these animals with deficient adrenals. The authors did not find that adrenalectomized rats succumbed to a very much smaller dose of morphine than normal rats

—F A H

Über ADRENALIN Stuber, Russmann & Proebsting, München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1281

The authors have invented a new chemical method for the estimation of extremely small quantities of adrenalin. No details are given —J K

ADRENAL incretory and direct nervous secretory mechanism of hyperglycemia by splanchnic excitation. Experimental dissociation (Double mécanisme, glyco et adrénalino—secrétoire de l'hyperglycémie par excitation splanchnique. Dissociation expérimentale) Tournade (A) & Chabrol (M), Compt rend Soc de biol (Par), 1922, 86, 315-316

By means of an anastomosis between the right suprarenal vein of one dog (B) with the jugular of another (A) (see Endocrinol, 6, 285), it is possible to divert the blood of B into the circulation of A. There is then an increase in glycemia in both dogs. This is interpreted as demonstrating that hyperglycemia is due to the secretion of adrenalin in the case of A, and an effect on the liver in the case of B —T C B

A note on ADRENALIN hyperglycemia in man Ulrich (H L) & Rypins (H), J Pharmacol & Exper Therap (Balt), 1922, 19, 215-220

The authors were not able to produce polycythemia by adrenalin through loss of fluid into the liver as observed in dogs. However, on account of the severe systemic reaction, they were not able to use more than 0.33 cc of a 1:1000 solution intravenously in a 70 kilo man. This is about 1/180 of the dose which has been used in dogs. Adrenalin hyperglycemia in man is not explained on the basis of a change in blood concentration, because it is independent of such change —F A H

Influence of ADRENIN in DIABETES (Über die probatorische Adrenalinwirkung beim Diabetiker) Veil (W H) & Reiser (A), Deutsches Arch f klin Med (Leipz), 1922, 139, 235-244

When adrenalin is injected subcutaneously in normal persons, four blood sugar curves may be constructed, as follows: (1) a flat line, gradually rising to ± 160 mg in 1 hour, (2) a line with a sharp angle, reaching 160 mg in ± 30 minutes, 180-230 mg in ± 1 hour and then falling rapidly, (3) a high, long plateau, (4) a high line, rapidly rising, and after 10 minutes a rapid fall. The first two are normal lines, 3 and 4 are seen in increased irritability of the

nervous system ("Reizkurven") The authors then constructed curves in 12 cases of diabetes In one very light case, curve 1 was seen In 5 very nervous cases, types 3 or 4 were seen All the patients died In 6 cases a different curve was found First there was a very slight decrease, then a retarded rise, the maximum blood sugar being reached in 4 hours in one case These 6 cases with nervous manifestations were found to have *secondary diabetes* One patient had an encephalomalacia of the medulla oblongata, one a tumor of the base of the brain, one probably had a pineal disease, one an encephalomalacia from arteriosclerosis, a fifth developed diabetes after apoplexy and the last had syphilis The authors further studied the vasomotor reaction in diabetes after ingestion of adrenalin The reaction was normal in cases with normal blood sugar curves In serious cases (with "Reizkurven") the intensity was much diminished—as was seen in the cases of secondary diabetes Glycosuria occurred in slight degree or not at all in cases showing normal blood sugar tracings, in cases with "Reizkurven" there was a parallelism between the amount of blood sugar and glucosuria In cases of secondary diabetes with retarded glycemia reaction there was no relation between blood sugar and glucosuria The glucosuria was sometimes very marked when the glycemia was low, and high glycemia was not always accompanied by glycosuria Further injection of adrenalin increased the acidity of the urine, acidosis occurred or was increased and the CO₂ tension in the alveolar air was diminished —J K

The action of ADRENAL on the skin glands of the toad Wastl (H),
Ztschr f Biol (Munchen u Leipz), 1922, 74, 77-80

The subcutaneous injection of 1 cc of a 1 10,000 or 1 20,000 solution of adrenaline induces secretion of the skin glands of the toad —Chem Abst, 10, 1623

The pathology of DIABETES 1 Hydropic degeneration of the islets of Langerhans after partial pancreatectomy Allen (F M),
J Metabolic Research (Morristown), 1922, 1, 5-41

This is the first of a series of papers by the author on the pathology of experimental diabetes In it are reported the histological changes in the cells of the islets after partial removal of the pancreas Hydropic degeneration is proved to be a specific diabetic condition produced by overstrain of the cell function The first positive vacuolation appears in from four days to one week and this is maximal at the end of one month After six or eight weeks the beta cells may disappear entirely as the animal becomes completely diabetic, whereas the alpha cells show no changes The difference in the behavior of the partially and totally depancreatized animals taken together with this difference in appearance of the two types of cells indicates that the beta cells furnish the internal

secretion lacking in diabetes, while the alpha and other cells of the pancreas furnish material essential for other life processes This is the first anatomical evidence of injury to cells due to overstrain of their incretory function and is offered as a means of diagnosing active diabetes histologically—I M

The pathology of DIABETES 3 Nervous influence in the etiology of experimental diabetes Allen (F M), J Metabolic Research (Morristown), 1922, 1, 53-73

The object of this investigation was to study the effect of nervous influences in diabetes by various procedures Normal and diabetic animals exposed to various forms of shock failed to show any changes attributable to this factor The Bernard puncture in a partially depancreatized animal caused fatal glycosuria Enervation and grafting studies showed the sugar tolerance to be undisturbed by the procedure, and grafted pancreas showed the specific vacuolation of the islands under the same conditions as in the pancreas with nerves and other connections intact—I M

The pathology of DIABETES 4 The rôle of hyperglycemia in the production of hydropic degeneration of islands of Langerhans Allen (F M), J Metabolic Research (Morristown), 1922, 1, 75-88

The purpose of this series of experiments was to determine the effects of different blood sugar levels upon the cells of the islands In a portion of the experiments the effects of intense hyperglycemia, produced by intravenous or oral administration, was studied on normal and experimentally diabetic dogs with negative results Although glycosuria was produced, no hydropic changes or vacuolation occurred in the cells Hypoglycemia, produced by phlorizin administration, had no effect in producing or repairing changes in the cells The author concludes that there is some other factor than hyperglycemia that is responsible for the hydropic changes in the diabetic islets—I M

The pathology of DIABETES The influence of circulatory alterations upon experimental diabetes Allen (F M), J Metabolic Research (Morristown), 1922, 1, 89-95

This group of experiments was intended to show any possible relation of circulatory or vasomotor disturbances to the pathology of diabetes By operative methods the blood supply to and from the pancreas remnant in experimental animals was regulated and varied No changes in the appearance of the cells or in the functional activity of the islands could be observed following such procedures—I M

Experiments on carbohydrate metabolism and DIABETES 4 Dea-
trose-nitrogen ratios in partially DEPANCREATIZED dogs Allen
 (F M) & Wishart (Mary B), J Metabolic Research (Morristown), 1922, 1, 97-107

This paper deals with the D N ratio, especially in depancreatized animals. Not all animals with the pancreas completely removed show a permanent 28:1 ratio, but the authors believe that those not showing the total ratio are as completely diabetic as those with this ratio. Some only partially depancreatized animals show the total ratio. The D N ratio cannot, therefore, be an infallible test as to whether the pancreas has been completely removed. A total D N ratio even for a short time in the partially depancreatized dogs indicates a fatal outcome. In human cases of diabetes this is not so, perhaps because a part of the disturbance is functional and capable of correction, whereas it is all organic in case of the experimental diabetes. Partially depancreatized animals can be distinguished from those totally depancreatized by a smaller loss in total sugar and nitrogen, by a lower total basal metabolism, by better nutrition and by much longer lives.—I M

The pathology of DIABETES 6 PANCREATITIS in the etiology
of experimental diabetes Allen (F M), J Metabolic Research
 (Morristown), 1922, 1, 165-192

The experiments reported in this paper were undertaken to reproduce more nearly the clinical pathology of diabetes in the presence of large masses of apparently healthy pancreatic tissue. It has previously been observed by the author that spontaneous diabetes occasionally occurs in old and obese dogs and exceptionally in experimental animals in which atrophy and fibrosis have occurred in large pancreatic remnants. In the present experiments a successful attempt was made to reproduce these conditions by causing an acute pancreatitis by mechanical trauma or occlusion of the pancreatic circulation for a time. Marked power of tissue regeneration was observed in most cases, but in a few fibrosis and atrophy occurred with clinical diabetes as an end result. The conclusion is drawn that fibrosis may occur in the pancreas as evidence of past injury, but does not indicate a progressive inflammatory condition. The fate of the islands depends upon the occurrence of hydropic degeneration or its not occurring—hence the value of prolonged dietary control.—I M

The pathology of DIABETES 7 Microscopic studies of the PAN-
CREAS in clinical diabetes Allen (F M), J Metabolic Research
 (Morristown), 1922, 1, 193-219

This paper considers in some detail the microscopic findings in the pancreas in human diabetes and compares them with the picture in experimental diabetes in animals. While most frequently the

human diabetic pancreas at autopsy does not show the typical hydropic degeneration of the islet cells seen in experimental diabetes, hydropic changes probably have occurred at an early stage with subsequent repair or regeneration. Acute infections or toxic processes or functional strains must increase the intensity of the hydropic degeneration and so increase the severity of the diabetes progressively. Identical degrees of hyperglycemia and glycosuria cause more rapid downward progress in diabetic children than in diabetic adults, perhaps because of the greater susceptibility of the child's pancreas to functional strain. With hyperglycemia but a glycosuria the diabetes of childhood becomes worse, but in adults the condition tends to remain stationary or to improve. All pancreas sections examined showed some signs of abnormality in the islands, as fibrosis, hydropic or hyaline degeneration, or quantitative reduction in the islet tissue. Severe cases with marked diabetic symptoms at time of death showed hydropic changes, whereas old, severe cases without diabetic symptoms, in which the patient died of starvation from lack of food tolerance, showed a scarcity of islands and fibrosis. Functional deficiency apparently does not cause death, and further organ changes can be halted or delayed by dietary control.—I M

The pathology of DIABETES 8 The microscopic pathology of the PANCREAS in 570 unselected hospital cases. Allen (F M), J Metabolic Research (Morristown), 1922, 1, 221-250

This paper deals with the pathology of the pancreas in 21 diabetic and 549 clinically nondiabetic cases. All of the diabetic and 48 per cent of the nondiabetic cases showed some kind of lesion of the pancreas. Many of the latter group had associated cirrhosis of the liver, gall stones and syphilis. Focal necroses, acute pancreatitis, hemorrhages, fatty infiltration and fibrosis constitute the chief lesions in the nondiabetic cases. Diminution in the number of islets and hydropic or hyaline degeneration of the remaining islets with or without diffuse fibrosis is the specific condition of diabetes, although a large functional element is also recognized.—I M

The pathology of DIABETES 9 Literature and discussion. Allen (F M), J Metabolic Research (Morristown), 1922, 1, 251-279

This paper summarizes the author's observations on the pathology of diabetes. It is pointed out that the pancreas is one of the most commonly diseased organs in the body from infections local and generalized, intoxications of various kinds by way of the ducts, the blood or the lymphatics, from neoplasms, etc. There is said to be no uniform pathological change pathognomonic of diabetes. A uniform functional alteration of the islands is probable. Hydropic changes in the islet cells indicate active diabetes and occur especially in severe youthful cases. The author holds that the majority of diabetic cases are not inherently progressive and can be controlled indefinitely by proper treatment. The chief causes

of a forward course in any case are intercurrent infections and hydropic changes from over-taxed function The author denies a selective preservation of the islands of Langerhans after pancreatic duct ligation—I M

Alcohol in the DIABETIC diet Allen (F M) & Wishart (Mary B), J Metabolic Research (Morristown), 1922, 1, 281-306

This investigation, in which ethyl alcohol was employed to increase the total caloric value of the diabetic diet, was undertaken to further test Allen's original contention that the diabetic subject is limited in his "power to metabolize calories as such" as well as to metabolize carbohydrates It is held that the assimilative power is injured or diminished when the total caloric tolerance is exceeded by any food, even fat and alcohol It was found that increases above the caloric tolerance in the total caloric intake due to fat or alcohol increase alone (the total available glucose remaining the same), caused hyperglycemia, glycosuria and acetonuria Ethyl alcohol is not converted within the body into glucose or acetone The increased caloric intake in these fairly severe diabetic patients failed to cause gain in weight or nutrition, but, on the other hand, lowered the assimilation power still further—I M

(DIABETES) Treatment of diseases of metabolism with mineral waters (Behandlung von Stoffwechselkrankheiten mittels Thermalwasser) von Benczur, Deutsche med Wchnschr (Berl), 1922, 48, 543

Health resorts may have effective results only in fat patients with diabetes, and this is usually slight Drinking water with laxative properties may also be useful—J K

(DIABETES) The distribution of blood sugar in the circulating blood (Ueber die Verteilung des Blutzuckers im stromenden Blute) Csáki (L), Wien Arch f inn Med, 1922, 3, 459-468

The author estimated the blood sugar with Bang's micromethod To obtain blood plasma, 5 cc of fresh blood were centrifugated for 5 minutes and the plasma was immediately used to estimate the sugar In this way the blood sugar and plasma sugar could be compared, while defibrination and the adding of anti-coagulation substances was avoided Csáki proved that the corpuscles contain little or no sugar In diabetes, however, the corpuscles may contain even large quantities of sugar When in normal persons the blood sugar is increased, the corpuscles remain sugar free In diabetes the corpuscles have a marked permeability for sugar This difference between normal and diabetic blood is not changed by the absence or presence of acetone or diacetic acid—J K

DIABETIC edema and acidosis (Diabetisches Oedem und Acidose) Foldes (E), Wien Arch f inn Med, 1922, 3, 469-498

Many patients with diabetes show fluctuations in their weight, due to varying degrees of edema. Every day the author gave to 9 patients ± 50 gm of sodium bicarbonate. Six of these patients had diabetes with or without mild acidosis, one had Graves' disease, the two others suffered from combined sclerosis (sclerose en plaques). None developed edema and none showed spontaneous variation of weight. In cases with marked acidosis the ingestion of comparatively small doses of sodium bicarbonate was often followed by an increase in weight and edema. There are, however, cases with severe acidosis in which no edema is seen after ingestion of NaHCO_3 . Many of these cases showed very severe polyuria. When the acidosis disappears, the possibility of edema from ingestion of NaHCO_3 disappears also. The author formulates the following as a law: "Without acidosis, no diabetic edema." When a patient with acidosis has no edema, edema may develop from three causes: (1) sudden increase of the acidosis, (2) diminishing of diuresis (as is seen on fasting days or when a strict diet is given), (3) when much salt (NaHCO_3) is given. The refractive index of the blood serum sinks when edema develops, and rises when edema disappears. This proves that the protein concentration of the serum changes when edema occurs. The author was able to prove that this was not caused by changed quantity of protein but only by variations of the quantity of water. In cases of diabetic edema, hydremia always exists. It is probable that acidosis also has an influence on the kidneys and facilitates the development of edema. In diabetes without acidosis the size of the red corpuscles is the same as in normal persons. In severe acidosis they are generally larger than in health. When such patients ingest NaHCO_3 until the urine becomes alkaline or until its acidity is largely diminished, the size of the corpuscles diminishes also. The average size of the corpuscles is thus a method for measuring acidosis. The author has proved that the corpuscles show an increased size in diabetics in whom edema easily develops. Foldes has found, too, that when so much NaHCO_3 is given that the urine becomes alkaline, no edema is seen, edema may develop when less NaHCO_3 is given, so that acidosis does not disappear.—J K

The use of oats in DIABETES (Het gebruik van haver bij suikerziekte) Foyer (A), *Nederl Tijdschr v Geneesk* (Amst), 1922, 66, (I) 1420-1423

A short general review. Nothing new.—J K

The presence of pyrocatechinic acid in normal and DIABETIC urine (Eine Untersuchung über das Vorkommen von Brenztraubensäure in normalen und Diabetikerharn) Fricke (R), *Ztschr f physiol Chem* (Berl u Leipz), 1922, 119, 39-45

Negative results.—F S H.

(DIABETES) Glycemia and glycosuria Graham (G), Lancet (Lond), 1921, i, 951-955

This is the first of a series of three lectures delivered before the Royal College of Physicians on the subject of diabetes. This paper deals almost entirely with a review of the physiological aspects of carbohydrate metabolism. In discussing the fate of the sugar present in the blood, the author describes experiments made upon himself in which he showed fairly marked variations in individual response to a given dose of sugar at different times, for example, before and after a holiday. The difference in tolerance for different sugars is pointed out also. Regarding the mechanism regulating the amount of sugar in the blood, he discusses the glucose mobilizing activity of the adrenals, the thyroid and the hypophysis and the antagonistic activity of the pancreas. Of particular interest is the review of Cohnheim's work on the substance in muscle tissue found necessary for sugar storage, of the work of Dakin and Dudley on a substance necessary to prevent conversion of muscle sugar into lactic acid (anti-glyoxose) and of Clark's observations on the substance in muscle which enables them to oxidize sugar—I M

Treatment of DIABETES with diet and mineral waters (Diabetes therapie durch Diat und Mineralwasserkur) Graul, Deutsche med Wchnschr (Berl), 1922, 48, 543, Klin Wchnschr (Berl), 1922, 1, 917

A vegetarian diet is the best for diabetes. The water of Neuenahr brings about effective results in diabetes, not only while the patient is in Neuenahr, but also later—J K

Modern views on DIABETES (Diabetes in moderner Beleuchtung) Heiberg (K A), München med Wchnschr, 1922 69, 731-733

In children with diabetes, harmless infections (bronchitis, a simple cold) may markedly diminish carbohydrate tolerance. When a diet rich in calories is given, much more food passes through the body without being properly digested than when a diet poor in calories is given. Therefore, the best diet would be one as poor as possible in calories. Treatment with alimentary rest, as taught by the American investigators, shows enormous progress in the treatment of diabetes—J K

Simplification of the Woodyatt method for calculating the optimal DIABETIC diet Holmes (W H), J Am M Ass (Chicago), 1922, 78, 22-23

Four tables are presented to simplify the calculation of the optimal diabetic diet, as recently recommended by Woodyatt
—W M A

Methods of precision in DIABETES A new instrument John (H J), J Am M Ass (Chicago), 1922, 78, 103-105

The use of a vacuum bleeding tube containing picric acid solution for blood sugar determination is described It is claimed that it is useful and reliable even when a delay of two or three days intervenes between the collection of the specimen and its analysis, thus making available distant laboratory facilities —W M A

Vitamines and DIABETES (Vitamine und Diabetes) Klotz & Hopfner, Munchen med Wchnschr, 1922, 69, 465-466

Vitamines influence metabolism The calcium metabolism in rickets is improved when fresh extracts from sweet potatoes, turnips or carrots are given In an experiment upon one patient, a girl of 12, the authors found that extracts from sweet potatoes in not too large quantities diminished the sugar in the blood and urine, but that yeast had no influence However, Borutteau (Biochem Ztschr (Berl), 1918, 88, 420) proved by much more extensive experimentation the existence of antidiabetic substance in these vegetables and in yeast also —J K

Polyuria and DIABETES (De polyurie bij suikerziekte) Koopman (J), Nederl Tijdschr v Geneesk (Amst), 1922, 66, (I) 1338

A short note Data reported in Endocrinol, 1922, 6, 48

The dietetic treatment of DIABETES (Einige Bemerkungen uber die diatetische Behandlung des Diabetes) Krehl (L), Fortschr d Med (Berl), 1922, 40, 309-310

In diabetes, restriction of food is necessary, not only fat, carbohydrates and proteins but also vegetables (salad) must be limited It is very important that the patients be weighed regularly Not only should a diet be selected that keeps the urine sugar free, but it is highly important to study the blood sugar and to give a diet in which, if possible, blood sugar is normal —J K

High blood pressure and DIABETES (Hypertoni och sockersjukdom) Kylin (E), Hygiea (Stockholm), 1922, 84, 49

Kylin determined the blood pressure in 71 cases of diabetes mellitus Some of his readings were obtained while the patients were still in the hospital, others, when the patients returned to have their pressure taken Most observations were made in the afternoons In the diabetics under 40 years of age, the blood pressure was normal, while after 40 hyperpiesis was the rule Thus 75% had a systolic pressure of over 160 mm of Hg, and 50% had 180 and over Kylin suggests that high blood pressure and reduced carbohydrate tolerance go hand in hand, and since some cases of hypertension also have lymphocytosis he is inclined to believe that

high blood pressure is due to an endocrine deficiency, possibly a hypofunction of the sex glands—D J G

Fasting treatment of DIABETES (*Les cures de jeune chez les diabétiques*) Labbé (M), Bull et mém Soc méd d hop de Par, 1921, 45, 689-699

In diabetes where denutrition has not occurred the fasting method of treatment leads to good results. The glucosuria disappears, no acidosis appears if it has not already been present, although some slight acetone and diacetic acid excretion may take place. There is some loss of nitrogen and body weight. The arterial pressure is but little less during the treatment. In cases where emaciation is present the fasting treatment affords only a passing relief—F S H

Overnutrition with fat and alcohol in severe DIABETES Leclercq (F S), J Metabolic Research (Morristown), 1922, 1, 307-317

The authors attempted to determine the effect of increasing the total caloric intake by administration of alcohol and fat in two fairly severe cases of diabetes. The intake of protein and carbohydrate was kept at a constant level, representing the tolerance of the patients for these foods. In no instance was the weight or strength increased and no beneficial clinical change was found to take place. After a few days of improvement, the patients began to feel weak and uncomfortable. Hyperglycemia followed both fat and alcohol ingestion, and so did not help for long. A further impairment of assimilation resulted, due to excess of calories—I M

(DIABETES) The inhibiting influence of lumbar puncture on glycosuria (*L'influence frénatrice de la ponction lombaire sur la glycosurie*) Lhermitte (J) & Fumet (C), Compt rend Soc de biol (Paris), 1922, 86, 479-480

The subtraction of a small amount of spinal fluid by lumbar puncture in diabetics determines a notable diminution in the excretion of glucose completely independent of all modifications of regime. This action is temporary, but may last several days—T C B

Xanthoma DIABETICORUM report of case Lyon (D M), Edinb M J, 1922, 28, 168

Apart from the skin lesion Lyon's case presents several points of unusual interest. All the symptoms and the examinations of the blood and urine suggested a serious type of diabetes mellitus. The patient had polyuria reaching 7,000 cc, glycosuria of 5 per cent, and daily waste of about 300 gm carbohydrate, high fasting level of the blood sugar, 0.388 per cent, and very low carbohydrate tolerance as shown by the greatly exaggerated postprandial rise in the blood sugar. There was obvious difficulty in dealing with the fats

ingested Such a serious state of affairs in a man, aged 25, would suggest a very bad prognosis, and yet he returned to almost perfect health From this it would seem that in making a prognosis less weight should be given to the evidence of the severity of the disease and more to the amount of improvement that the patient is capable of under treatment This improvement has been maintained for at least nine months —J Am M Ass, 78, 1761

Hypertonia and DIABETES (Über Hypertonie und Zuckerkrankheit Marañón (G), Zentralbl f innere Med (Leipz), 1922, 43, 169-176

As both diabetes and hypertonia are mostly seen in patients over 40, one might believe that age was the cause of the coincidence It is remarkable that in many patients there is marked hypertonia some time before glucosuria is found Marañón states that in these cases hypertonia often gradually diminishes when the diabetes develops When a patient of about 40 begins to show an increased blood pressure and blood sugar, a decreased carbohydrate tolerance, and a changed reaction after injection of adrenalin, it is probable that diabetes will set in Fourteen out of 22 cases of hypertonia without glucosuria showed hyperglycemia There are cases of hypertension in which this symptom is only temporary and disappears with treatment or even without treatment Patients with hypertonia and adiposity often become diabetic, it is the same with those with hypertonia who complain of severe itching Some of these patients have hyperglycemia It may be the same in case of furunculosis or neuralgia The author concludes that in a certain number of cases of diabetes there exists a "preglycosuric stage" of hypertension with other symptoms, such as itching, neuralgia, furunculosis, etc —J K

The pathology of DIABETES 2 Granule stains of the islands of Langerhans of the diabetic and non-diabetic pancreas Martin (W B), J Metabolic Research (Morristown), 1922, 1, 43-52

In this paper the author describes the alpha and beta cells making up the islets and the special staining technique by which the two types are distinguished The eccentrically placed alpha cells with their oval vesicular nuclei and basophilic granules are greatly in the minority, while the centrally placed beta cells with rounded nuclei and acidophilic granules surround the blood capillaries and make up the greater part of the islets Four stages of alteration in the cells are described as taking place in diabetic animals with gradual disappearance of the beta cells Corresponding stages are not found in all cases of human diabetes, the beta cells appearing normal in some, which indicates that some functional alteration must be assumed as the basis of diabetes in man —I M

(DIABETES) Sugar metabolism (Beitrag zum Zuckerstoffwechsel)
Meier, München med Wchnschr, 1922, 69, 138-139

The author gave his patients, on an empty stomach, 20 gms of glucose and one hour afterwards, 100 gms more. In normal persons after the dose of 100 gms no further increase in blood sugar is seen, but a second increase was observed in patients with icterus, nitrobenzol poisoning, obesity due to endocrine insufficiency, and serious neurosis. In diabetes, even a second dose of 10 gms caused a marked rise.—J K

DIABETES und Balneologie Minkowski (O), Deutsche med Wchnschr (Berl), 1922, 48, 475-477, Klin Wchnschr (Berl), 1922, 1, 917

A stay in a health resort may have a good effect in diabetes. To explain this, Minkowski suggests the following. The general condition of the patient is improved by favorable hygienic, climatic, psychical influences, etc., which have an influence on the diseased organs. Mineral water increases the production of certain enzymes or hormones, influences the velocity of reactions ("Reaktionsgeschwindigkeit") and contains substances, which can, at least partly, take the place of substances, the want of which causes diabetes. Since, however, these things are purely theoretical, it is advisable to send patients only to those health resorts in which a good diabetic treatment is prescribed.—J K

DIABETES mellitus en DIABETES INSIPIDUS Munk (J), Nederl Maandschr v Geneesk (Leiden), 1921, 2, 253-268

A description of 4 cases. The first was a girl of 4 with extremely malignant diabetes mellitus. The second was a girl of 5½ with diabetes insipidus cured by the oral administration of hypophysis tablets. The third and fourth were girls of 5½ and 9 with diabetes mellitus. The last two had "diathèse neuro-arthritique" in the family.—J K

The importance of the alimentary experiment, especially the reaction of glycemia, for the functional study of SUGAR METABOLISM (Ueber die Bedeutung des Alimmentarversuches, speziell der "glykamischen Reaktion" für die funktionelle Prüfung des Zuckerstoffwechsels) Offenbacher (R) & Hahn (R), Arch f Verdauungskr (Berl), 1922, 29, 193-219

The authors estimated the amount of blood sugar with the stomach empty, then 50 gm of glucose in 300 gm of tea was given and every hour the sugar in the blood and urine was determined. In some cases no changes in the blood sugar were seen after one hour but in other healthy persons a moderate increase was still seen. These were usually nervous persons. In neurasthenia a rise

during the first hour of $\pm 100\%$ or more was seen and in the second hour this rapidly fell to, or even under, the normal blood sugar content. In 3 cases of Graves' disease glucosuria was seen. All of the 7 cases of this disease examined had low blood sugar content on an empty stomach, 6 showed a very marked rise (much more than 100%) of blood sugar the first hour after the ingestion of the glucose. In all cases the hyperglycemia disappeared after two hours. In only one case was the blood sugar high on an empty stomach, and in this case the blood sugar remained unaltered by ingestion of 50 gm of carbohydrate—J K

A chart for the rapid estimation of Woodjatt's optimal DIABETIC diet. O'Hara (D), J Am M Ass (Chicago), 1922, 78, 1124

With the body weight and glucose tolerance known, the chart permits a rapid calculation of the optimal arrangement of the protein, fat and carbohydrate in the diet—W M A

Factors in development of DIABETIC acidosis (Ueber die Faktoren die für die Entwicklung der Azidose bei Diabetes von Bedeutung sind) Petrén, München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1280

In health as well as in diabetes, acidosis is caused by a lack of carbohydrate in the diet. In diabetes, however, acidosis occurs also when the patient takes more than a certain amount of nitrogen in the form of proteins. Proteins raise the blood sugar, fats have no influence—J K

Syphilitic DIABETES Rathery (F) & Fernet (P), Bull et mém Soc méd d hôp de Par, 1922, 46, 661-667

A report of a case of diabetes cured by antisyphilitic treatment—F S H

Treatment of DIABETES (Behandlung des Diabetes) Richter (P F), Ztschr f ärztl Fortbild (Jena), 1922, 19, 33-41

A general good review, without new data—J K

Pathogenesis and treatment of DIABETES (Wesen und Behandlung des Diabetes) Schreiber, München med Wchnschr, 1922, 69, 139

No new data are given—J K

Experiments on carbohydrate metabolism and DIABETES The influence of glucose ingestion on diuresis and blood composition in non-diabetic and diabetic persons. Sherrill (J W) & John (H J), J Metabolic Research (Morristown), 1922, 1, 109-129

The authors studied the effect of glucose ingestion on urinary output, blood volume, hematocrit readings, hemoglobin and blood

sugar in 19 persons, a part of whom were diabetic and the remainder normal. They found that in the majority of cases oliguria and a decrease in hematocrit reading accompanied the hyperglycemia, whereas diuresis followed upon the appearance of a hydremic plethora as the blood sugar returned to the normal level. Hemoglobin values decreased with the hyperglycemia, as did the hematocrit, but both returned to normal following the diuresis. In one control case 10 gm of sodium chloride was ingested with similar results.

—I M

Dietetic treatment of DIABETES (*Die Aufgaben der Diätbehandlung in der Diabetestherapie*) Strausz (H), *Deutsche med Wchnschr* (Berl), 1922, 48, 546-549

A general review —J K

A peculiar disturbance of carbohydrate metabolism and its relation to DIABETES (*Über eine eigenartige Störung des Kohlenhydratstoffwechsels und ihre Beziehungen zum Diabetes mellitus. Eine klinisch-experimentelle Studie*) Wagner (R) & Parnas (J K), *Ztschr f d ges exper Med* (Berl), 1921, 25, 361

The authors have investigated a case of glycosuria in a girl of 8½ years who had been under observation since the age of 4. The principal physical sign was a greatly enlarged liver. It was that the morning urine gave an intense reaction for acetone compounds. With the administration of both starch and sugar there was glycosuria. The remarkable feature of the case was that, on examination of the blood, it was found that during fasting the fluid was entirely free from sugar. After food, an extreme hyperglycemia took place. In the fasting stage injections of adrenalin did not produce the hyperglycemia which occurs in normal subjects under similar conditions. Hence the disturbance is not due to a mobilization of glycogen, but is due to a lack of mobilizable carbohydrate. In this case the administration of protein, lactates, glycerine, and amino-acids after fasting raised the content of sugar in the blood. Thyroid in fairly large doses was without effect with larger doses lipemia, lipuria, and staetorrhoea occurred. During one day the normal quota of sugar appeared in the blood. The authors look upon the case as one of azoosamylia, i e., a lack of function on the part of the liver to store up sugar in the form of glycogen. On the other hand, the regulating mechanism is absent which in the normal fasting subject catabolizes protein in order to keep the sugar content of the blood at its normal level, and in cases of diabetes leads, in spite of the absence of carbohydrates in the food, to a hyperglycemia. This process, however, can be replaced by the administration of thyroid, and thus shows the importance of this gland for sugar metabolism in that the thyroid regulates the endogenous protein metabolism and prepares this protein for the formation of sugar. In the relation of pancreas and thyroid, the latter acts as a

brake to excessive pancreatic activity It is difficult in the present case to make out clearly the relations of pancreas, liver and thyroid It is possible that with the dysfunction of the liver there is an independent disturbance of the thyroid which leads to an inhibition of endogenous protein breakdown, or the lack of liver function and activity of the thyroid are determined by a disturbance of the pancreas —Med Sc , 6, 161

DIABETES INSIPIDUS of infundibular origin *Anatomo-clinical study (Le diabète insipide d'origine infundibulaire Etude anatomo-clinique)* Lhermette (J), *Compt rend Soc de biol (Paris)*, 1922, 86, 579-581

Whether diabetes insipidus is of hypophyseal or nervous origin is still under discussion Hitherto we have possessed no facts absolutely demonstrating the origin of polyuria in man, because the majority of observations are either incomplete, or too complex to be utilized The present paper describes a case of polyuria in a man of 65, under observation for 17 months He had chronic aortitis and incipient tabes The daily quantity of urine was 4 to 4.5 liters There was a positive Wassermann in the blood and cerebro-spinal fluid Specific treatment was of no avail The autopsy showed a syphilitic basilar meningitis involving the tuber cinereum and the infundibulum The hypophysis was intact There was granular degeneration of the cells of the nuclei of the tuber, chromatolysis of the paraventricular nuclei and the supra-chiasmatic nuclei were vacuolated The hypophysis, thyroid and suprarenals were unaltered These facts justify the conclusion that polyuria in man, as in experimental animals, may be due to lesions in the vegetative center of the base of the brain and not to lesions of the hypophysis There is a short discussion by G Roussy —T C B

DIABETES INSIPIDUS Lorant, *München med Wchnschr*, 1922, 69, 796, *Klin Wchnschr (Berl)*, 1922, 1, 1280

When purin free food was administered to patients with diabetes insipidus, thus causing nitrogen equilibrium, their uric acid metabolism became abnormally high A short note —J K

The INCRETION of the tonsils (Zur Frage der inneren Sekretion der Tonsillen) Amersbach & Königfeld, *Klin Wchnschr (Berl)*, 1922, 1, 501, *Deutsche med Wchnschr (Berl)*, 1922, 48, 542-543

Fleischmann has stated that the tonsils have an endocrine function because it is possible to extract from them a substance which reduces AuCl_3 The authors consider this observation as of no significance because nearly all tissues contain such substances —J K.

Principal questions in ENDOCRINOLOGY (Prinzipielle Fragen zur Lehre von der inneren Sekretion) Asher (L), Klin Wchnschr (Berl), 1922, 1, 105-108

A general review without new facts —J K

(ENDOCRINE GLANDS) Pathology of the sympathetic (Pathologia do sympathico) Barros (F), Arch Rio Grandenses de Med (Porto Alegre, Brazil), 1922, 3, 51-56

A general review of the interrelations of the endocrine glands, the sympathetic nervous system and various pathological manifestations —F S H

ENDOCRINE factor in dental caries Broderick (F W), Proc Roy Soc Med (Lond), 1922, 15, 22-40

Hypotheses not supported by experimental evidence
—Physiol Abst , 7, 49

The action of thallium on the ENDOCRINE organs (Die Wirkung des Thallium auf den endokrino System) Buschke (A) & Peiser (B), Klin Wchnschr (Berl), 1922, 1, 995

More than 20 years ago Buschke demonstrated that animals lost their fur when thallium was given Since there were no changes in the skin the author believed that thallium had a central action These studies have been repeated and it has been proved that when thallium is given to young animals growth is retarded or ceases completely In adult animals sexual desires disappear and there exists a complete atrophy of the testicle In the adrenals no adrenalin, or only traces of it are found Sometimes cataracts were seen, perhaps due to an abnormal function of the parathyroids It is not yet certain whether changes occur in the thyroid —J K

(ETIOLOGY) Myasthenia gravis A therapeutic and clinical study Dana (C L), J Am M Ass (Chicago), 1922, 78, 261-263

Fourteen personal cases are reported with a general discussion of the disease The clinical and pathological grounds for belief in an endocrinal etiology are briefly referred to, without experimental evidence —W M A

The influence of x-rays on the ENDOCRINE glands (Der Einfluss der Röntgenstrahlen auf inkretorische Drüsen) David, Klin Wchnschr (Berl), 1922, 1, 1025

No specific data are given —J K

Influence of x-rays on the ENDOCRINE ORGANS (Ueber die Beeinflussung endokriner Drüsen durch Röntgenstrahlen) David, München med Wchnschr , 1922, 69, 526

No details are given The necessity of exact dosage of x-rays is stated —J K

(ENDOCRINE ORGANS) Glioma and status hypoplasticus Diamantopoulos (H S), Klin Wchnschr (Berl), 1922, 1, 708

In a boy of 13 with hypoplastic gonads and polyuria, post-mortem examination showed glioma which had destroyed the corpora mammillaria and tuber cinereum, hypoplasia of the lymph tissue, and atrophy of the thyroid and testicles No particular changes in the hypophysis were found —J K

Functional diagnosis of diseases of the ENDOCRINE organs (Funktionelle Diagnostik der Erkrankungen der Blutdrusen) Falta, Klin Wchnschr (Berl), 1922, 1, 1028

Some general remarks without new data —J K

ENDOCRINE ORGANS in woman (Innersekretionische Vorgänge bei der Frau) Franz, Deutsche med Wchnschr (Berl), 1922, 48, 544, Klin Wchnschr (Berl), 1922, 1, 970

Menstruation and ovulation are quite different things Menstruation is caused by the endocrine function of the ovary X-radiation of the ovary before menstruation has no influence on menstruation, when the ovaries are exposed to x-rays after menstruation the next menstrual period is missed In pregnancy the size of the thyroid and the pars anterior of the hypophysis may increase enormously Hypertrophy of the mammae and lactation do not depend upon the ovary The only ovary preparation of therapeutic value is ovoglandol, and this only because of its large calcium content.

—J K

(ENDOCRINE) Intoxication in adults, arteriosclerosis and organotherapy with "animasa" (Nährschaden Erwachsener, Arteriosklerose und deren organo-Therapeutische Beeinflussung durch "Animasa") Funck (C), Arch f Verdauungskr (Berl), 1922, 29, 167-170

The author believes that a pathological protein metabolism may be responsible for many cases of diabetes, hypertonia, glycosuria and beginning arteriosclerosis Extract of the intima and media of blood vessels is combined with a substance procured by destruction of the protein of blood and is called 'animasa' When given by mouth it brought very good results in many cases of arteriosclerosis One case is quoted in which the blood pressure sank from 205 mm to 160 mm No convincing data are adduced —J K

The influence of CO baths on the INTERNAL SECRETION of the skin (Die Wirkung der Kohlensäuren Bäder die innersekretorische Funktion der Haut) Groedel, Deutsche med Wchnschr (Berl), 1922 48, 544, Klin Wchnschr (Berl), 1922, 1, 1281

CO₂ baths have good effect in endocrine disturbances (diabetes, Graves' disease) A relation between the endocrine glands and the skin is highly probable as many endocrine disturbances produce cutaneous symptoms When extracts of skin are injected they produce the same symptoms as extracts of adrenals Therefore, the author concludes that the endocrine function of the skin is proved, that probably the CO₂ baths primarily act on the internal secretion of the skin and that this produces a change in the other endocrine glands —J K

(ENDOCRINE ORGANS) *Experimental studies on the pathogenesis of gout (Experimentelle Beiträge zur Pathogenese der Gicht)* Gudzent & Keeser, *Ztschr f klin Med (Berl)*, 1922, 94, 1-11

During their studies on gout the authors estimated the quantity of uric acid in different organs They found that the fatty tissue did not contain uric acid, very small quantities were found in the thyroid, muscle and lung, there was more in the testicle, bile, kidney and brain, large quantities were found in the liver, spleen and pancreas —J K

Glimpses into ENDOCRINOLOGY Hamilton (W F), *Canad M Ass J*, 1922, 12, 209-214

A case is cited of a male, aged 25, 4 feet 7 inches in height, and weighing 76 pounds Development was normal until he was ten years old For fifteen years he had headache and development was slow, especially of the genitalia Autopsy showed a tumor of the pituitary, choroid plexus, atrophy of the thyroid and testes, adiposity and effeminate characteristics A second case, a male, at 5 years of age showed characteristics of a young adult in voice, teeth and genitalia Operation revealed a tumor of the adrenal cortex The patient again became practically a normal child A third case, that of a girl 8 years old, is cited For two years she had typical symptoms and laboratory findings of diabetes insipidus Two years later, symptoms of a brain tumor developed Four years after onset a post-mortem showed a tumor occupying the space of all the structures in the circle of Willis The author says the case is not at all in favor of the view that diabetes insipidus is a hypophyseal syndrome

—J H

Histological studies on the ENDOCRINE ORGANS in psychical disturbances (*Histologische Untersuchungen der innersekretorischen Drüsen bei psychischen Erkrankungen*) Fauser (A) & Heddacus (E), *Klin Wchnschr (Berl)*, 1922, 1, 374

Will be published in detail in the *Ztschr f d ges Neurol u Psychiat* —J K

Amphibian metamorphosis and INTERNAL SECRETIONS Huxley (J S) & Hogben (L T), *Proc Roy Soc (Lond)*, 1922, 93 B, 36-53

Metamorphosis takes place in Salamandra and Triton larvae in dilute iodine. In Axolotl, thyroid feeding causes more rapid metamorphosis (with exophthalmos), especially in young larvae, than does enforced air breathing, this is accelerated by rise of temperature. Free iodine or feeding on prostate or anterior pituitary, has no effect. In Necturns, thyroid diet for 7 months did not lead to somatic change. Pituitary diet (posterior lobe or whole gland) causes temporary dilatation, then contraction, of dermal melanophores in Axolotl, adrenal medulla produces temporary complete contraction. Administration of mammalian pineal causes transient contraction of these cells in frog tadpole, but not in Axolotl. The authors think probably the pineal ought to be admitted as a part of the endocrine system —Physiol Abst

Influence of the ENDOCRINE organs on cell oxidations and heat regulation of the body (Wirkung von Inkreten auf die Zelloxydationen und den Warmehaushalt des Organismus) Lipschutz, München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1282

Cell respiration was exactly measured. Extract of pancreas from an animal during hibernation diminished the respiration, extract of pancreas of a dog has no influence. Thyroid and pineal extracts increase respiration, thymus and cortex of adrenal decrease it. These last preparations diminish the temperature, while thyroid and pineal increase it —J K

The influence of the ENDOCRINE ORGANS on the calcium content of human serum (Ueber den Kalziumgehalt des menschlichen Blutserums und seine Beeinflussung durch Störungen der inneren Sekretion) Leicher, München med Wchnschr, 1922, 69, 331 and 797, Klin Wchnschr (Berl), 1922, 1, 1282

In Graves' disease and after ingestion of thyroïdin the calcium content of the serum sinks, in myxedema it is high, after ingestion of hypophysis it sinks, in a case of tumor of the hypophysis it is high, ingestion of ovary causes decrease, castration causes increase, injection of adrenin causes a decrease and ingestion of parathyroid, an increase —J K

(ENDOCRINE GLANDS) Treatment of epilepsy Lopes (R de S), Brazil-med (Rio de Jan), 1922, 1, 141

Souza Lopes here discusses the accessory factors responsible for the epilepsy, the irritable motor and sympathetic systems, the toxemia, and the abnormal functioning of the endocrine glands. He describes the different signs of abnormal conditions in these various fields as the main problem in treatment of epilepsy —J Am M Ass, 1922, 78, 1853

(**ENDOCRINE GLANDS**) The next great advance in medicine Macallum (A B), Canad M Ass J, 1922, 12, 202-208

The opinion is given that the next great advance will be made by biochemists. The endocrine interest in this article is found in the discussion on constipation in which it is said that bacteria enter the blood stream and there ensues a hypertrophy of the *pituitary* and the adrenals with more or less atrophy of the other endocrinous glands—J H

(**ENDOCRINOLOGY**) Animal experimentation and dental research Mellanby (May), Dental Rec (Lond), 1922, 42, 1-12

A lecture dealing with previous work by the authoress and others on dogs, etc. Endocrine hypotheses still lack experimental evidence—Physiol Abst, 7, 49

(**ENDOCRINE GLANDS**) Glandular syndromes (Syndromas glandulares Nonohay (U de), Arch Rio-Grandenses de Med (Porto-Alegre, Brazil), 1922, 3, 56-57

A brief description of forms that are not new—F S H

Some aspects of **ENDOCRINE therapy** Patton (A B), J Med Ass Georgia (Augusta), 1922, 11, 23

A brief general discussion of the present status of organotherapy. The author concludes "We know enough of the endocrines to have great faith in their ultimate effectiveness when we shall have learned to use them safely, and to realize that we really know little about them at present, that they are potent and dangerous, and that our information about them should come from the laboratory and clinic and operating room, and not from the manufacturer's advertising department"—R G H

(**ENDOCRINE GLANDS**) Organ extract glycosurias (Ueber das Vorkommen von Organextraktglykosurien) Schenk (P), Ztschr f d ges exper Med (Berl), 1921, 24, 208-213

A report of the effect of the intramuscular injection into dogs of extracts of the thyroid, testis, thymus, ovary, corpus luteum, placenta and the various parts of the *pituitary*. In no case was glycosuria produced. The *pituitary* preparations and the extracts of the thyroid and thymus caused slight hyperglycemia

—F S H

Possible **hormonic action of the CILIARY BODY** (Su d'una possibile azione ormonica dell'epitelio ciliare) Scalingi (N), Riforma med (Napoli), 1922, 38, 345-346

The author advances his hypothesis on the following premises (a) the well known secretory activity of the ciliary epithelium, histologically and biologically demonstrated, (b) the non-existence of

a steady production of endocular fluid (function previously attributed to the ciliary process), (c) the hormonal functional connection between sympathetic and hormonal products, and, on the other hand, the arrested development of the eye following a spontaneous as well as an experimental lesion of the cervical sympathetic, (d) the deficient developments of the eye, or, at least, of its anterior segment, following certain inflammatory processes of early youth, (e) the bulbar atrophy and the sympathetic ophthalmia following "only" severe lesions of the ciliary processes —G V

INNERE SEKRETION und Balneotherapie Schlayer, Deutsche med Wchnschr (Berl), 1922, 48, 544, Klin Wchnschr (Berl), 1922, 1, 970

Diseases of the pineal, parathyroids, hypophysis, adrenals and thyroid cannot be treated by balneotherapy except in light cases, especially of Addison's disease, tetanoid attacks, etc. A good climate is often effective in slight cases of hyperthyroidism, chlorosis and osteomalacia —J K

(ENDOCRINE ORGANS) Fetal chondrodystrophia in a calf (Zur Frage der Chondrodystrophia fetalis beim Kalbe) Seifried, Munchen med Wchnschr, 1922, 69, 417

In this case of fetal chondrodystrophia in a calf the hypophysis was normal but all other endocrine glands histologically showed a defective development. In the thymus the cortex, when compared with the medulla, was abnormally large, the Hassall's corpuscles were very small and their number was diminished. The number of eosinophil and plasma cells in the thymus was also very small. According to Schridde this would prove a defective secretion of the organ —J K

Influence of ENDOCRINE GLANDS on the sensibility to spasms (Weitere tiereperimentelle Untersuchungen uber den Einfluss endokriner Drusen auf die Krampfahigkeit) Specht, Klin Wchnschr (Berl), 1922, 1, 811, 1128

A short note. The removal of the thyroid, testicle or adrenals has no influence on the sensibility of the animal to spasms

—J K

Progressive LIPODYSTROPHY Strauch (A), J Am M Ass (Chicago), 1922, 78, 1037-1038

A case of this rare condition is reported and the various theories of its etology, including endocrinopathies, are discussed

—W M A

(ENDOCRINE GLANDS) Essential itching as a clinical symptom of pluriglandular insufficiency (Das essentielle Hautjucken als klinisches Symptom der multiplen Blutdrusenerkrankung)

Szondi (L) & Haas (L), *Munchen med Wchnschr*, 1922, 69, 584-585

Ten cases of pruritus are described in which no cause of the itching was found. In 6 cases there was a typical pluriglandular insufficiency. The 4 other patients also showed endocrine symptoms. One patient had exophthalmic goiter, positive Grafe symptom, and Neisserian oophoritis. A second patient had a small thyroid with hard nodules. A third had dysmenorrhea, no sexual desires and a hypoplastic thyroid. The fourth showed only a hypoplastic thyroid and a want of sexual desires. Itching may be an extremely disagreeable symptom of an endocrine dysfunction. The author suggests that it may be explained by a hyperirritability of the sensitive nerves caused by toxic products of metabolism. This hyperirritability becomes itching in places that undergo regular irritation. Organotherapy gave only temporary relief.—J K

(ENDOCRINE ORGANS) Influence of organotherapeutic preparations on carbohydrate tolerance (*Contributo allo studio della influenza dei prodotti opoterapici sulla tolleranza degli idrati di carbonio*) Travaglini (V), *Gazz d osp (Milano)*, 1922, 42, 1200

The pluriglandular theory of diabetes is the most probable. Therefore, polyphagia, polydipsia, tachycardia with inclination towards arrhythmia are symptoms of an increased function of the sympathetic system and may perhaps be due to hyperadrenalism. Though opotherapy does not cure diabetes, in some cases it may have some effect. In cases of typical pancreatic diabetes, injections of extract of pancreas (or extract of almonds which, as Farmachidis has shown, has the same influence) may have some influence on metabolism. The author believes that muscular exercise, ingestion of yeast, thyroid, opium, liver preparations and antipyretic drugs are all sometimes useful.—J K

ENDOCRINES and sympathetic Vercellini (G), *Minnesota Med (St Paul)*, 1922, 5, 211-216

A general philosophic review.—R G H

(GONADS) The ENDOCRINE functions of the female reproductive organs Vincent (S), *Lancet (Lond)*, 1922, ii, 303-305

An excellent brief review of our present knowledge of the subject, including discussions on the effects of extirpation of the ovaries at various ages, in man and also in the lower animals, the transplantation of the ovaries, extirpation of the corpus luteum, and the relation of the corpus luteum to the gravid uterus. The article (which is an abstract of the Ingleby lectures delivered at the University of Birmingham in 1921) is conservatively written, as may be judged from this sentence in the opening paragraph: "A biologist has only to discover a group of cells whose function is not clear

and it is instantly charged with that of internal secretion, a medical man need only find some baffling symptom or syndrome, and forthwith the magical word 'hormone' relieves him of all further responsibility for investigation"—E N

Correlation of the ENDOCRINE glands (Korrelation der Blutdrüsen)

Wagner (R), Wien klin Wchnschr, 1922, 35, 352

A girl of 10 months had a tumor of the liver and a most remarkable disturbance of carbohydrate metabolism. On an empty stomach there was scarcely any blood sugar, after the ingestion of carbohydrates an enormous hyperglycemia was seen. Adrenalin did not produce a rise of the blood sugar. Thyroidin, when given repeatedly, produced hyperglycemia, lipemia and lipuria. A fat free diet produced an xerosis of both eyes. The author believes the disease to be a hepatogenous azoosmia (Naunyn) with hypothyroidism.

—J K

Correlation of the ENDOCRINE glands Wagner (R) & Parnas

(J K), Med Klin (Berl), 1922, 18, 137

The girl of 10 seemed to have chronic interstitial hepatitis, the liver was very much enlarged, and in addition there was an odor of acetone about her when fasting, and there is glycosuria after ingestion of starch and sugar, but no sugar is found in the blood, fasting, although ketone bodies abound. After eating sugar and starch, the acetone disappeared, but intense glycosuria followed. This same sequence occurred day after day. Under thyroid treatment, lipemia, lipuria and steatorrhea developed. Wagner and Parnas theorize that the main disturbance in this case is the lack of the ability to form and store glycogen in the liver. In some respects the condition is like that of a mild diabetes, but it differs materially from the latter when sugar is not being supplied from without. There is no formation of sugar from the body reserves. But this takes place when thyroid treatment is given. This seems to suggest that the thyroid is in control of this function. They theorize further that the pancreas presides over the sugar metabolism, through the liver it checks the mobilization of glycogen, through the thyroid it influences the formation of sugar anew. The removal of the pancreas thus removes the brake on both these functions, and complete experimental diabetes is the result.—J Am M Ass, 78, 1174

The importance of ENDOCRINOLOGY in normal and pathological physiology (Die Ergebnisse der Lehre von der inneren Sekretion für die normale und pathologische Physiologie) Weil (A), Deutsche med Wchnschr (Berl), 1922, 48, 559-562

A short but excellent review without new data.—J K

Constitution and ENDOCRINE ORGANS (Konstitution und endokrines System) Wuth (O), München med Wchnschr, 1922, 69, 392-394

A general review without new data The author states the importance of the endocrine organs to the physical and psychical constitution Especially in psychiatry should more attention be given to these organs —J K

Tuberculosis and glands of INTERNAL SECRETION (*Tuberculosis e ghiandole a secrezione interna*) Zibordi (D), *Riforma med* (Napoli), 1922, 38, 295-298

The author reports his experiments on guinea pigs in regard to tuberculous infection after removal of the thyroid, of the genital glands, and of the thyroid and genital glands The removal of the thyroid alone did not cause any difference in the spreading of the infection, the removal of the testis did not sensibly slow the process The removal of both testis and thyroid and ovary and thyroid, while not modifying the process in males, succeeded in rendering very slow and torpid the process of infection in females The removal of ovary only showed a slight slowing of the process A discussion follows on the presumed opposite action of the male and of the female genital gland on the thyroid, which would bring about hypofunction in males and hyperfunction in females

—G V

Treatment of ENDOCRINE adiposity (*Behandlung der endokrinen Fettsucht*) Zondek (H), *Klin Wehnschr* (Berl), 1922, 1, 999-1000

A good general review without new facts —J K

ENDOCRINE adiposity (*Ueber endokrine Fettsucht*) Zondek (H) & Loewy (A), *Munchen med Wehnschr*, 1922, 69, 796, *Klin Wehnschr* (Berl), 1922, 1, 1280

In hypophyseal adiposity basal metabolism is not diminished In cases of local adiposity, as they may be seen in light endocrine disturbances (castration, pregnancy, Graves' disease, etc) a high, though not abnormally high, quantity of oxygen is used, but in one case of adiposity with Graves' disease enormous quantities were used In these cases thyroid therapy had no effect In ordinary cases of endocrine adiposity, however, thyroidin is very active Thyroid preparations in which the proteins have been decomposed, such as thyreoglandol or thyroidopton, are absolutely inactive in endocrine adiposity —J K

Development of human germ cells, etc (*Über die Bildung der menschlichen Geschlechtszellen und die Vorgeschichte der menschlichen Leibesentwicklung*) Friedenthal (H), *Arch f Rassen-u Gesellsch-Biol* (Liepz & Berl), 1921, 13, 257-276

Not of endocrine interest —A T R

(OVARY) The oestrous cycle in the mouse Allen (E), Am J Anat (Phila), 1922, 30, 297-371

A study based upon more than ninety mice It was found that external signs are unreliable criteria of oestrous in mice The presence of cornified cells in the vaginal smear is a much more accurate indication When these cells appear in masses, ovulation has usually occurred Characteristic changes in vaginal and uterine epithelium are described These are accompanied by periodic extrusion of nuclei from the epithelial cells of the oviduct Ovulation is not always spontaneous in virgin or unmated mice It is held that the corpora lutea have no primary causative relation to oestrous changes in the genital tract The conclusion is drawn that the presence of maturing ova in large follicles is the cause of prooestrus and oestrus, and that the removal of the ova at ovulation (or their atresia if this fails to occur) is the primary cause of the degenerative changes of the metoestrus —W J A

(GONADS) Pseudo-hermaphroditism in male Cetacea (Le pseudo-hermaphroditisme tubaire chez les Cétacés mâles) Anthony (R), Compt rend Acad d sc (Par), 1920, 171, 1398-1399

The almost constant occurrence of a greatly developed utriculous masculinus in some species of male Cetacea coincides in general with the poorly defined secondary sexual characteristics, and possibly with the absence of interstitial tissue in the testes, although only a single testis has been examined The author names other orders in which there is regularly a persistence in the male of a considerable part of the Müllerian ducts —A T R

INTERNAL SECRETION of the OVARY (Sur la sécrétion interne de l'ovaire) Athias (M), Arch internat de physiol (Liège & Par), 1921, 18, 296-306, abst Physiol Abst, 7, 52

A critical dissertation in which it is concluded that it is impossible at the present time to determine with certainty the specific parts of the ovary which function in producing specific hormones —R G H

(GONADS) Observations on the normal and pathological histology of the interstitial cells of man and mammals (Bemerkungen zur normalen and pathologischen Histologie der Zwischenzellen des Menschen und der Säugetiere) Benda (C), Arch f Frauenk u Eugenik (Leipz), 1921, 7, 30-40

There is first given a general yet concise statement of the development, structure and significance of the interstitial cells (i c) of the gonads but more particularly of the testis The origin is mesenchymal, in the opinion of the author As a rule, but not invariably, degeneration of the tubules of the testis is accompanied by an increase in the interstitial cells In syphilitic lesions of the

A general review without new data The author states the importance of the endocrine organs to the physical and psychical constitution Especially in psychiatry should more attention be given to these organs —J K

Tuberculosis and glands of INTERNAL SECRETION (*Tuberculosis e ghiandole a secrezione interna*) Zibordi (D), *Riforma med* (Napoli), 1922, 38, 295-298

The author reports his experiments on guinea pigs in regard to tuberculous infection after removal of the thyroid, of the genital glands, and of the thyroid and genital glands The removal of the thyroid alone did not cause any difference in the spreading of the infection, the removal of the testis did not sensibly slow the process The removal of both testis and thyroid and ovary and thyroid, while not modifying the process in males, succeeded in rendering very slow and torpid the process of infection in females The removal of ovary only showed a slight slowing of the process A discussion follows on the presumed opposite action of the male and of the female genital gland on the thyroid, which would bring about hypofunction in males and hyperfunction in females

—G V

Treatment of ENDOCRINE adiposity (*Behandlung der endokrinen Fettsucht*) Zondek (H), *Klin Wchnschr* (Berl), 1922, 1, 999-1000

A good general review without new facts —J K

ENDOCRINE adiposity (*Ueber endokrine Fettsucht*) Zondek (H) & Loewy (A), *München med Wchnschr*, 1922, 69, 796, *Klin Wchnschr* (Berl), 1922, 1, 1280

In hypophyseal adiposity basal metabolism is not diminished In cases of local adiposity, as they may be seen in light endocrine disturbances (castration, pregnancy, Graves' disease, etc) a high, though not abnormally high, quantity of oxygen is used, but in one case of adiposity with Graves' disease enormous quantities were used In these cases thyroid therapy had no effect In ordinary cases of endocrine adiposity, however, thyroïdin is very active Thyroid preparations in which the proteins have been decomposed, such as thyreoglandol or thyroïdopton, are absolutely inactive in endocrine adiposity —J K

Development of human germ cells, etc (*Über die Bildung der menschlichen Geschlechtszellen und die Vorgeschichte der menschlichen Leibesentwicklung*) Friedenthal (H), *Arch f Rassen-u Gesellsch -Biol* (Liepz & Berl), 1921, 13, 257-276

Not of endocrine interest —A T R

(OVARY) The oestrous cycle in the mouse Allen (E), Am J Anat (Phila), 1922, 30, 297-371

A study based upon more than ninety mice It was found that external signs are unreliable criteria of oestrous in mice The presence of cornified cells in the vaginal smear is a much more accurate indication When these cells appear in masses, ovulation has usually occurred Characteristic changes in vaginal and uterine epithellum are described These are accompanied by periodic extrusion of nuclei from the epithelial cells of the oviduct Ovulation is not always spontaneous in virgin or unmated mice It is held that the corpora lutea have no primary causative relation to oestrous changes in the genital tract The conclusion is drawn that the presence of maturing ova in large follicles is the cause of prooestrus and oestrus, and that the removal of the ova at ovulation (or their atresia if this fails to occur) is the primary cause of the degenerative changes of the metoestrus —W J A

(GONADS) Pseudo-hermaphroditism in male Cetacea (Le pseudo-hermaphroditisme tubaire chez les Cétacés mâles) Anthony (R), Compt rend Acad d sc (Par), 1920, 171, 1398-1399

The almost constant occurrence of a greatly developed utriculous masculinus in some species of male Cetacea coincides in general with the poorly defined secondary sexual characteristics, and possibly with the absence of interstitial tissue in the testes, although only a single testis has been examined The author names other orders in which there is regularly a persistence in the male of a considerable part of the Müllerian ducts —A T R

INTERNAL SECRETION of the OVARY (Sur la sécrétion interne de l'ovaire) Athias (M), Arch internat de physiol (Liège & Par), 1921, 18, 296-306, abst Physiol Abst, 7, 52

A critical dissertation in which it is concluded that it is impossible at the present time to determine with certainty the specific parts of the ovary which function in producing specific hormones —R G H

(GONADS) Observations on the normal and pathological histology of the interstitial cells of man and mammals (Bemerkungen zur normalen and pathologischen Histologie der Zwischenzellen des Menschen und der Säugetiere) Benda (C), Arch f Frauenk u Eugenik (Leipz), 1921, 7, 30-40

There is first given a general yet concise statement of the development, structure and significance of the interstitial cells (i c) of the gonads but more particularly of the testis The origin is mesenchymal, in the opinion of the author As a rule, but not invariably, degeneration of the tubules of the testis is accompanied by an increase in the interstitial cells In syphilitic lesions of the

testis he found no interstitial cells, but between the necrotic areas were functional tubules and fairly large groups of these cells. They are fairly numerous in cachexia. In inguinal retained testes there are usually very few, while in typical cryptorchism they are most often greatly increased. In hermaphroditism, the interstitial cells are mostly found in the testicular part of the ovotestis. In a recently reported case of typical virilism there were none. In another case (masculine externally except for well developed mammary glands) the author found many interstitial cells in the testicular portion while the ovarian part contained a distinct corpus luteum. Older cases are similarly reviewed. A case is given of a 19 year old external masculine pseudohermaphrodite (feminine in appearance) from whom one of the two testes was removed. This contained typical testicular tissue, some portions of which were either infantile or contained degenerating and adenomatous tubules, but between the tubules of the pathological areas were large groups of typical interstitial cells. None were found in the ovary of a newborn feminine hermaphrodite. Four cases of homosexuality are detailed but there were no distinctive features.

In a case of Basedow's disease the interstitial cells were numerous and rich in fat. In a case of acromegalia there appeared to be regressive metamorphosis of these cells and some degeneration in the tubules. In a case of infantilism in a 20 year old man in whom the testes were not apparently infantile, there were only a few interstitial cells that were at all typical and these lacked fatty droplets. The testes of a 38 year old man with a teratoma in the sella turcica and great reduction of the hypophysis were infantile as to germinal epithelium and not a single typical interstitial cell could be found. Most of the descriptions are from personal observations. Benda concludes that while the normal and pathological anatomy of the interstitial cells of the testis undoubtedly contain many interesting problems, up to the present time no general uniformity as to their meaning is obtainable from the morphological data. Only a few references are given—A T R

(GONADS) The puberty gland (Die Pubertatsdrüse) Berberich, München med Wchnschr, 1922, 69, 331

The author believes that the interstitial cells have an unknown endocrine function. The sexual-endocrine function depends upon the spermatogenous cells. No details or reason are given—J K

(TESTES) Operative attempts at organic rejuvenation or treatment of genitoglandular dystrophy (Os ensaios operatorios de rejuvenescimento organico e a terapeutica da dystrophia genito-glandular) Castro (A de), Prensa Méd Argentina (Bs Aires), 1922, 8, 289

An excellently presented discussion. Testicle grafting is indicated for three purposes: to rejuvenate, to ameliorate the symptoms

of castration, or to lessen the manifestations of genitoglandular dystrophy In the second case the indication is simply the replacing of a missing organ In the third case testicle grafting is merely the best resource available Observations on three cases of eunuchoidism are reported —B A H

(GONADS) Relations between MENSTRUATION and different organs (Wechselbeziehungen der Menstruation zu den einzelnen Organen) Daude, Deutsche med Wchnschr (Berl), 1922, 48, 544

Of no endocrine interest —J K

The SEX character as pathogenic factor (Konskaraktarens patogenetiska betydelse) Ehrstrom (R), Finska Läk-sällsk handl (Helsingfors), 1921, 63, 1-15

In a preceding paper the author pointed out that there is a difference in frequency of "nephrosclerosis" in the two sexes No such difference occurs in "nephritis" and "nephrosis" Stimulated by these findings the author has made a study of the literature concerning the relative frequency of different diseases in the sexes He comes to the conclusion that the exogenic factors very often do not sufficiently explain this difference There must be a variation of disposition and resistance due to the sex A combination of exogenic factors and disposition is sometimes to be seen The relation between man and woman as regards sporadic struma is 4 1, endemic struma, 2 1 Thus the exogenic factors in the endemic are strong enough to impress also the individuals with greater resistance The sexual factors are of very great importance and those who try to reduce the difference between man and woman to a minimum are all false prophets —H B

Development of a myoma after transplantation of an OVARY (Myomentwicklung nach Ovarientransplantation) Fleischmann C), Zentralbl f Gynäk (Leipz), 1922, 46, 82-83, Klin Wchnschr (Berl), 1922, 1, 348, München med Wchnschr, 1922, 69, 101

One woman suffered from amenorrhea and sterility, another from myoma of the uterus Half of each of the two ovaries were transplanted One ovary contained a small cyst, the other a corpus luteum In the patient with amenorrhea the uterus enlarged after the operation, then a myoma developed, and menstruation, which the patient had not had for 16 years, returned —J K

(GONADS) The problem of homosexuality (Das Problem der Homosexualität) Gaupp (R), Klin Wchnschr (Berl), 1922, 1, 1033-1038

A general review without new data —J K

A case of **TESTICLE** transplantation with control after three months
(Ein Fall von Hodentransplantation mit Kontrolle nach einem Vierteljahr) Forster (W), München, med Wchnschr, 1921, 68, 106-107

A man of 55 with precocious senility was troubled with lymphosarcoma of the neck. When he was cured with x-rays a testicle, taken from a man of 20 years with cryptorchism, was implanted into the abdominal wall. The operation had no effect on the senility and the man died 3 months afterwards from cachexia. Necropsy disclosed complete necrosis of the graft.—J K

Absence of **CORPORA LUTEA** in a case of atypical uterine hemorrhage Geist (S H), J Am M Ass (Chicago), 1922, 78, 1185-1186

A married woman of 28, mother of four children, had periods of several months' duration of alternating amenorrhea and menorrhagia. Examination of the tissues removed at operation revealed no pathological alterations sufficient to account for the condition except the absence of corpora lutea. The relation of the ovary to menstruation and pathologic bleeding is discussed. The conditions underlying the periods of amenorrhea are not considered.

—W M A

(**GONADS**) Sex intergradation (Untersuchungen über Intersexualität) Goldschmidt (R), Ztschr f indukt Abstammungs- u Vererbungs- (Berl), 1920, 23, 1-199

A highly technical discussion abstracted at length in Ber ü d ges Physiol, 1922, 11, 467-471.—R G H

Numerical analysis of the **OVARIES** of a healthy woman of 22
(Zahlenmassige Analyse der Ovarien eines 22 jährigen gesunden Weibes) Häggstrom (P), Upsala Läkaref Forh, 1921, 26, 1-52, J Aug Hammar Festschrift. Each article is paged separately.

The ovaries of an unmarried, healthy woman 22 years old who suddenly died of CO-intoxication were cut in sections 36 μ thick. Every 10th section was magnified 1 17 in the drawings. The borders of the sections, of the different parenchyma zones and of all the follicles, corpora atretica, lutea and albicantia being over 100 μ in size were indicated. The follicles were followed from section to section. The small follicles were drawn at a magnification of 1 200 in every 50th section. By measuring and counting the author obtained figures indicating the relation between the different parenchyma components and the absolute number of the follicles, the corpora lutea and atresia over 100 μ in size and finally the approximate number of the small follicles. The number of follicles was approximately 17,000 in the smallest and 250,000 in the largest ovary. The small follicles were most numerous, only

219 were over 100 μ in size. The values did not differ considerably when only every 100th section was counted. Of the follicles only 5 per 10,000 showed liquor folliculi. Two nuclei in one egg were found in every 416th follicle. The author points out that this figure agrees very well with the frequency of twins. Follicles with two ova were found only 5 times. The total number of the corpora atretica was approximately 12,000, most of them (9,000) being small. The percentage of corpora atretica of the small follicles was low (2%). On the other hand, the corpora atretica over 100 μ in size were 10 times as common as the intact follicles of the same size. The zona pellucida seems to be the most resistant component of the parenchyma and was found in every 4th of the corpora atretica. The number of corpora lutea was 9, 4 in one and 5 in the other ovary. The microscopic picture indicated that probably the bursting of the follicles had occurred alternately in the two ovaries. There were 48 corpora albicantia in the large ovary and 10 in the small one. Thus the follicles did not always burst alternately. The total number of corpora lutea and albicantia proves that the woman had menstruated at least 5 years before her death.—H B

Alimentary GLYCOSURIA as a diagnostic test (Die Alimenfare Glycosurie als diagnostische Probe) Hofbauer (J), Zentralbl f Gynäk (Leipz), 1922, 46, 348-351

Many years ago the author proved that alimentary glycosuria was a rather reliable diagnostic test for pregnancy. It was positive from the end of the second month, later on, during pregnancy, it might become negative again. These observations have been confirmed by newer studies of Frank and Nothmann and of Nurnberger. Hofbauer believes that the placenta stimulates the hypophysis and the thyroid and that therefore it is possible to consider this test as a test for the presence of a normally functioning placenta. Perhaps the disturbed function of the liver also plays a role in this test. It is remarkable that the ingestion of 200-300 gm will, in pregnancy, produce a "crise haemoclasique".—J K

(OVARY) Observations on the sexual cycle of the white rat Ishii (O), Anat Record (Phila), 1922, 23, 311-314

The author presents a summary of the outstanding features of his studies on the oestrous cycle. In certain points he differs from other recent authors. The first oestrous appears, according to Ishii, at an age of 32 to 40 days. The period of heat is distinguished as a shorter part of general oestrous, generally occurring at night. He denies that sterile copulation lengthens subsequent oestrous periods.

—W J A

ENDOCRINE aspect of female sterility Jacoby (A), Med Rec (N Y), 1922, 101, 239-241

The author reviews briefly the physiology of the uterus and ovaries, and urges that every case of sterility in which gross pathological conditions can be excluded warrants a careful study of the individual with a view to determining any malfunction of the endocrine system and the use of the indicated extracts for prolonged periods. He cites two cases which he believes illustrate the value of organotherapy in sterility under certain conditions. The first patient he believes to have suffered from deficient ovarian secretion. She had been married two years, without pregnancies. The administration of 5 grains of ovarian extract three times a day for two months was followed by pregnancy. In the second case, which the author thinks was one of deficient development of the ovary plus a diminished activity of the pituitary, he attributes the good results to the administration of ovarian extract in similar dosage, in addition to one-half mg of pituitrin, hypodermically, three times a week.

E N

(GONADS) Certain cases of hermaphroditism, with special reference to the interstitial cells (*Über einige Fälle von Hermaphroditismus, mit besonderer Berücksichtigung der Zwischenzellen*) Keussler H von), *Beitr z path Anat u z allg Path (Jena)*, 1920, 67, 416-436

Three subjects of hermaphroditism with female secondary characters, possessed testes with interstitial cells. The author interprets his observations as opposed to Steinach's theory of the "puberty-gland"—W J A

(GONADS) The reproductive glands and mental disorder with special reference to dementia praecox. Kirby (B H) & Gibbs (C E), *State Hosp Bull (Utica)*, 1921, 6, 147-158

An interesting general discussion is followed by a record of the size and consistency of the testes in 313 psychotics as determined by palpation. Random (alphabetical) selection of subjects was employed. The results are indicated in the subjoined table.

Variations in Size and Consistency of the Testes

	Number of cases	Abnormal size, per cent	Abnormal consistency per cent	Abnormal size and consistency, per cent
Dementia praecox	186	56	47	31
Manic-depressive	50	46	22	12
General paralysis	49	42	58	28

285

Columns showing abnormal size and abnormal consistency include cases showing both changes in the same individual as shown in last column. The unusually favorable situation of State Hospitals for post-mortem endocrine studies is emphasized.

—R G H

(GONADS) Ovariotestes in the goat (Ovariotestes bei der Ziege)
Krediet (G), Biol Zentralbl (Leipz), 1921, 41, 447-455

Hermaphroditism is fairly common in goats. Most cases are, however, pseudohermaphroditic. Of the twenty cases observed by the author in which the genitalia appeared feminine but the head and general habitus masculine, only three are taken up in detail. Two of these had gonads which contained both testicular and ovarian structures, but there were no typical ovarian stroma cells which could be called a female "puberty gland" (unless this was represented by theca interna cells or other elements), and yet the animal showed some female characteristics (e.g., gave considerable milk). In a third goat, 4 months old, there were no interstitial cells clearly recognized in the ovariotestes. The significance of such close association of male and female gonadal elements with reference to the Steinach's theories, mono- and bi-sexuality and to Lillie's theory of the cause of freemartins is discussed. The histological findings in the hypophysis of only one of the three goats is briefly stated. No references.—A T R

(GONADS) Transplantation of testicle and homosexuality (Hoden-
transplantation und Homosexualität) Kreuter (E), Zentralbl
f Chir (Leipz), 1922, 49, 548-550

Some years ago (see Endocrinol 1920, 4, 318) the author described the use of testicle transplantation after castration. He has now completely changed his opinion because the grafts nearly always become necrotic. In a previously normal patient who had been castrated on account of tuberculosis he grafted a testicle of a homosexual man. After the transplantation the patient sometimes had erections and his feelings remained heterosexual without the slightest trace of homosexuality. The effect of the transplantation on the physical symptoms of the castration was nil.—J K

(GONADS) Pregnancy and menstruation glycosuria (Schwangerschafts und Menstruationsglykosurie) Küstner (H), Klin
Wchnschr (Berl), 1922, 1, 312

It is well known that during the beginning of pregnancy the tolerance for sugar may be low. The author tried to determine whether this was due to the ovum. He found, however, that women sometimes have sugar in the urine even when the blood sugar is no more than 0.13 to 0.18 per cent. This occurs a few days before menstruation. It is probable that some relationship exists between pregnancy (and menstruation), glycosuria and the ovary.—J K

(GONADS) Development of the interstitial glands (Zur Entwicklung der interstitiellen Geschlechtsdrüse) Lahm, Klin Wchnschr (Berl), 1922, 1, 299. See also München med Wchnschr, 1922, 69, 485

The interstitial cells have a trophic function. In the testicle they arise from the epithelium. The secondary sexual characteristics depend upon the seminal cells.—J K

(TESTES) The significance of the thymus in the development of the male sex glands (*Die Bedeutung des Thymus für die Entwicklung der männlichen Keimdrüsen*) Leupold (E), *Beitr z path Anat u z allg Path* (Jena), 1920, 67, 472-491

The conclusion is reached that the testis is dependent, for its normal development, upon the combined influence of the thymus and the adrenal. It is held that the influence of the thymus upon the testis is through an effect upon the adrenal.—W J A

GONADS and growth (*Glandes génitales et croissance*) Lereboullet (M), *Progrès méd* (Par), 1922, 37, 137-140

A lecture discussing in a general way the relation of the gonads to growth.—R G H

New observations on the endocrine function of the interstitial cells of the mammalian TESTICLE (*Nouvelles observations sur la fonction endocrine des cellules interstitielles du testicule chez les mammifères*) Lipschutz (A) & Wagner (C), *Compt rend Soc de biol* (Paris), 1922, 86, 306-307

The theory of the endocrine function of the interstitial cells of the testicle has been attacked of late on the ground that eunuchoidism is possible even in their presence, the generative tissue accomplishing the endocrine function. In studying compensatory hypertrophy of the testicle after unilateral castration, it was observed that in animals castrated at about six weeks of age the penis was still infantile at six and a half months, while the testicles remaining weighed 85 per cent more than controls from the same litter. The tail of the epididymis was full of living spermatozoa. Somatic eunuchoidism is thus possible in the presence of complete spermatogenesis. In these eunuchs the interstitial cells showed marked differences. The nuclei were small, the protoplasm less abundant. In some places the cells were better developed. These observations demonstrate that well developed interstitial cells are a necessary condition for the endocrine function of the testicle.—T C B

(GONADS) The minimum amount of TESTICULAR substance necessary for the attainment of normal sexual character (*Ueber das minimum der Hodensubstanz, das für der Geschlechtsmerkmale ausreichend ist*) Lipschutz (A), Ottow (B) & Wagner (K), *Arch f d ges Physiol* (Berl), 1921, 188, 76-86

If 1% of the total testicular substance of a male guinea pig is left within the animal it suffices for the development of the normal somatic sexual characteristics. When 0.5% or less remains the ap-

pearance of the signs of total castration are retarded In testicular tissue there may occur a complete degeneration of the spermatogenic tissue after section of vas deferens, x-radiation or transplantation If partial castration is done before sexual maturity, spermatazoal ripening may occur The interstitial cells in a well vascularized testicular residue are markedly increased in number

—F S H

Interstitial cells in guinea-pig TESTIS Lipschütz (A), Ottow (B), Wagner (C), & Bormann (F), Proc Roy Soc (Lond), 1922, 93 B, 132-142

Hypertrophy of these cells is not compensatory, and it does not always occur after castration Whether it occurs is due to local conditions, the most important factor being blood supply The hypertrophy occurs markedly in the upper portion of the testis, which is better supplied with blood than the lower part —

—Physiol Abst

(GONADS) A case of true lateral hermaphroditism in man (Ein Fall von Hermaphroditismus verus lateralis beim Menschen) Losert (J), Beitr z klin Chir (Tübing) 1921, 122, 411-417

A 19 year old soldier was operated upon for inguinal hernia and cryptorchism Near the left inner inguinal ring was a 3x2 5x2 cm ovary, histologically it was essentially like that of a sexually mature woman It contained corpora lutea and follicles in all phases A small uterus and attached tube were also removed A careful description of these structures and related ligaments is given The left scrotal sac was empty, but the right contained a testis 2 5 cm in diameter with palpable epididymis and ductus deferens, from which a milky fluid could be obtained While spermatozoa were not found it appeared certain that there was a right testis The reactions of Florence and Barberio were negative The individual in general appeared and acted masculine and had fairly well developed external male genitalia, but there were some female characteristics, especially the well developed mammary glands, which commenced to enlarge at the age of 13 There were no indications of any menstrual periods Observations 1½ years after the removal of the ovary showed that there had been no increase in the size of the penis or in libido, but the mammary glands had decreased noticeably and were distinctly more flaccid Comparisons are made with six other cases on record, but no specific references to literature are given —A T R

(GONADS) Hermaphroditism (Über Hermaphroditismus) Mittasch (G), Beitr z path Anat u z allg Path (Jena), 1920, 67, 142-180

A case of pseudo-hermaphroditismus masculinus internus in an individual 54 years of age A rather comprehensive review of simi-

lar cases in the literature is given and the theoretical considerations are discussed —W J A

"All or none" law or the functional constant relative to the action of the TESTICLE as an endocrine gland (Loi du "tout ou rien" ou de constance fonctionnelle, relative à l'action du testicule considéré comme glande endocrine) Pézard (A), *Compt rend Acad de sc (Par)*, 1921, 172, 89-92

Subperitoneal grafting of portions of testis in castrated cocks leads to the development of secondary sexual characteristics if the weight of testis implanted is 0.5 gm or more. If the graft has a lower weight than this, the animal remains neuter. There is no intermediate state —*Physiol Abst*, 6, 75

Latent period in the experiments of TESTICULAR transplantation and the "all or none" law (*Temps de latence dans les expériences de transplantation testiculaire et loi du "tout ou rien"*) Pézard (A), *Compt rend Acad de sc (Par)*, 1921, 172, 176-178

After grafting testicular tissue in castrated cocks there is a latent period of 2 to 6 weeks, during which there is no difference between the animals and control cocks, which have been castrated without implantation of testicular tissue. Then comes a sudden divergence, and the grafted animals develop secondary sexual characteristics at a rapid rate —*Physiol Abst*, 6, 76

(GONADS) A cured case of homosexuality, treated by transplantation of a testicle (*Ein geheilter Fall von Homosexualität durch Hodentransplantation*) Pfeiffer (E), *Deutsche med Wchnschr (Berl)*, 1922, 48, 660-662

The patient was a man of 33. From his twenty-first to his thirtieth year no abnormal sexual desires were experienced. Then he dreamed of men and felt sexual excitement when in the presence of men. The pubic crines were of somewhat feminine type. The patient was operated upon for hernia and, unknown to him, a piece of testicle was ingrafted. Some weeks later the pubic scutcheon had increased in size and the patient not only had normal sexual desires but wished to marry —J K

Interstitial cell tumors of the TESTIS in bird hybrids (*Zwischenzellengeschwulste des Hodens bei Vogelmischlingen*) Poll (H), (*Beitr z path Anat u z allg Path (Jena)*), 1920, 67, 40-56

Hybrids produced by crossing the peacock and the guinea fowl exhibit a great development of interstitial cells amounting almost to tumor-like growths —W J A

(OVARY) Some aspects of vascular hypertonus Ritchie (H J), *M J Australia (Sydney)*, 1922, 1, 318-322

"The only type of hypertension in which endocrine imbalance has been proved to play a part is that met with in women about the climacteric, which often yields rapidly to the administration of extract of corpus luteum"—Quoted

(GONADS) Spermatogenic or interstitial cells (Geschlechtszellen oder Zwischenzellen) Romeis (B), Klin Wchnschr (Berl), 1, 960-964, 1005-1010, 1064-1067

This is the best of the many reviews on this subject. No new facts are given. According to the author, there is no valuable proof that the interstitial cells have an endocrine function. The problem of the interstitial cells still exists. Though it cannot be denied that these cells have a trophic function, it is not improbable that they still have other functions.—J K

The role of the lutein cells of the OVARY in certain uterine hemorrhages (Du rôle des cellules lutéiniques de l'ovaire dans certaines hémorrhagies utérines) de Rouville (G) & Sappey (P), Gynéc et Obstét (Par), 1922, 5, 1-38

The basis of this contribution is the histological study of 6 cases in which uterine hemorrhage was present, as compared with 6 in which there was no hemorrhagic tendency. The authors believe that menstruation is produced by an internal secretion of the lutein cells, either the so-called interstitial cells of the theca interna of atretic follicles or the lutein cells of the corpus luteum. They conclude, from the study of this small series, that hyperfunction of these cells produces pathologic uterine bleeding, that an average or normal function produces normal menstruation, and that a hypofunction of these cells entails amenorrhea. They emphasize that in the interpretation of the secretory capacity of these cells, the macroscopic appearance of the ovaries, whether they be cystic or not, is of no significance. Microscopic examination alone can give accurate information.—E N

(GONADS) The present view on Steinach's rejuvenation (Der gegenwärtige Stand der Steinachschen Regenerationslehre) Schmidt (P), Ztschr f ärztl Fortbild (Jena), 1922, 19, 14-17

A short general review. The author saw cases in which ligation of the vas deferens gave good results. No result may be expected, however, when the testicles of the patient show a marked senile atrophy. No case reports are given.—J K

(TESTES) Internal secretion and Steinach's rejuvenation (Innere Sekretion und das Steinachsche Verjüngungsproblem) Schmidtgen & Gruber, München med Wchnschr, 1922, 69, 98

A short general review without new data.—J K

The toxicity of PLACENTA lipoids Schonfeld (H E H), Arch f Gynæk (Berl), 1921, 115, 80-125

From the normal placenta various toxic substances may be isolated. Alcohol, acetone and glycerol extracts contain two substances which are insoluble in ether or petroleum ether. One substance produces convulsions in mice when injected subcutaneously. This substance is thermolabile, is activated by glycerol and is probably of the nature of an enzyme. In the same fraction there is a more thermolabile substance which causes uterine contractions. In extracts made with alcohol, ether, chloroform or other lipid solvents there are also 2 toxic substances, probably lipoids. One causes the formation of thrombin, particularly in the lungs and liver. The other substance is toxic for liver, kidney and endothelial cells. Several of these factors may play a role in the causation of eclampsia. The lipid content of the blood is high in the latter half of pregnancy and particularly high in eclampsia. At the slightest indication of eclamptic symptoms a detection of the lipid content of the blood would be of diagnostic value. Eclampsia may be considered as the result of an abnormal internal secretion of the placenta, with an accumulation of the secretion in the blood through lack of elimination through the liver or insufficient neutralization by other antagonistic endocrine substances, particularly the corpus luteum.

—Chem Abst, 10, 1272

The terminology of MENSTRUAL disorders (Über die Benennung der Menstruationsunregelmässigkeiten) Seltz (L), Zentralbl f Gynæk (Leipz), 1922, 46, 50-53

An interesting nomenclature of menstrual irregularities, but not of especial endocrine interest —E N

(GONADS) New investigations on the interstitial cells (Neue Untersuchungen über die Zwischenzellen) Stieve (H), Verhandl d anat Gesellsch (Jena), 1921, 30, Ergänzshfte z , Anat Anz , 1921, 54, 63-76

After an introductory definition of the "puberty gland," the enormous increase in the testis of *Colaeus monedula collaris* Drmd (European jackdaw), from the sexually quiescent stage of January to that of the breeding stage in April is described. Volumetric determinations show this increase to be, in one particular case, 418 times. This is largely due to an increase in the germinal epithelium and not to interstitial tissue. The increase may be as great as 1,000 times. In the male domestic goose Stieve found that fattening modifies the secondary sex characters and interferes with the onset of the breeding period and these in turn apparently injure the germinal cells, which degenerate, and increase the amount of interstitial tissue. Absolute figures of the amount of the various tissue in the testes is given as well as the amount per gram of body weight.

The increase in interstitial tissue coincided with a loss of secondary sex characters and the production of sterility. This, the author thinks, rather indicates that the internal secretion generally attributed to the interstitial cells comes from the germinal epithelium in the case of the goose—A T R

(HISTAMINE) Imidazolyethylamine and organ extracts I β -Imidazolyethylamine as a powerful stimulant of the gastric glands Popielski (L), Arch f d ges Physiol (Berl), 1920, 178, 214-236

In addition to its other effects, histamine acts as a strong stimulant of gastric secretion. When injected subcutaneously into dogs in amounts of 0.00021 gm per kgm of body weight secretion of gastric juice, of normal acidity and pepsin content, follows. The secretion begins within 10 minutes, attains its maximum within 45-60 minutes, maintains a high level for an hour, and then gradually diminishes in amount. The total amount secreted is about 3.75 cc per kgm. When administered by other routes the effects vary, oral introduction is without effect, and after intravenous injection the pancreatic, salivary, and lacrymal glands show increased activity. Section of the vagi, or the administration of atropine, does not essentially modify the secretory effect. It is suggested that the effective material in organ extracts which manifest the same properties is β -imidazolyethylamine—Chem Abst

(HYPOPHYSIS) Clinical study of a case of ACROMEGALY Benjamin (J E), J Am M Ass (Chicago), 1922, 78, 499-501

The case report of a young man is given in detail and is well illustrated with photographs and roentgenograms—W M A

Standardization of HYPOPHYSIS preparations (Wertbestimmung von Hypophysenpräparaten) Bijlsma, München med Wchnschr, 1922, 69, 796, Klin Wchnschr (Berl), 1922, 1, 1280

A short note. To determine the therapeutic value of hypophysis preparations the uterus of a guinea pig is used. This method, however, gives an idea only of its obstetrical use and not of its activity in the treatment of diabetes insipidus—J K

X-rays and tumors of the HYPOPHYSIS (Röntgenstrahlen und Hypophysentumoren) Biro, München med Wchnschr, 1922, 69, 722

A short note. Eight cases have been treated with large doses of x-rays. For over a year 6 of them have had no symptoms—J K

X-ray treatment of tumors of the HYPOPHYSIS and of HYPOPHYSEAL gynecological diseases (Ueber Hypophysenbestrahlungen bei Hypophysentumoren und bei gynäkologischen Erkrankungen

hypophysaren Ursprungs) Blumberg, München med Wchnschr, 1922, 69, 739-741

An exact description of the technical procedures in exposing the sella to the x-rays —J K

Experimental contribution to the problem of **HYPOPHYSEAL DIABETES** (Experimentelle Beiträge zur Frage des hypophysaren Diabetes) Brugsch (T), Dresel (K) & Lewy (F H), München med Wchnschr, 1922, 69, 796, Klin Wchnschr (Berl), 1922, 1, 1280

The innervation of the hypophysis is not certainly known. Weed, Cushing and Jacobsen have found that innervation comes also from the plexus carotid and that stimulation of the superior cervical ganglia after section of the sympathetic causes glucosuria. The authors could not confirm this, if the experiment as described by Cushing is carried out, the blood sugar is diminished. The existence of a hypophyseal diabetes has never been proved —J K

(**THYROID**) Some aspects of exophthalmic goiter Campbell (J M H), Quart J Med (Oxford), 1921, 15, 55

A study of the signs and symptoms, etiology, prognosis and distribution in England and Wales of 127 cases of exophthalmic goiter, treated at Guy's Hospital between 1908 and 1917. This study contains nothing new, but is of interest from a statistical viewpoint —F C P

Erythropoietic function of the **HYPOPHYSIS** (Erythropoïèse dans l'hypophyse) Collin (R) & Baudot (J), Compt rend Soc de biol (Paris), 1922, 80, 596-598

Histological. It is thought that if the conditions described are found in other mammals than the guinea pig (the animal studied), we may conclude that the embryonic hypophysis has a hemato-poietic function —T C B

Studies on the effect of diet on the weight of the **HYPOPHYSIS** and **THYROID** gland of the albino rat, and on the action of their extracts on the isolated small intestine Degener (Lyda M), Am J Physiol (Balt), 1922, 60, 107-118

This research was undertaken to determine the effect of different diets on the weight of the thyroid and hypophysis and on their extracts, using isolated intestine as an index. In one series three different diets were used, oatmeal, vegetables, and meat, respectively. In another, potassium, iodide and thyroxin were used in addition. Normal diet was fed to the controls. The body weights in all the groups were low, but the controls were heavier by about 5 gms. All the glandular weights were low for the body weights. The oatmeal thyroids were heavier than the controls by 1 mgm,

the hypophysis, by 2 mgm. In the vegetable group the thyroid was heavier by 4 mgm., due to one unusually large male. In the meat group the thyroid was heavier, the hypophysis was not altered. As for the activity of the extracts, there seemed to be no difference between the thyroids of the test and of the control animals. In the oatmeal and vegetable groups the extract of the hypophysis caused contraction of the isolated intestinal strip. The control always caused relaxation. Extracts of the pars anterior caused contractions, of the pars nervosa, relaxation. It is suggested that in the results from oatmeal and vegetable diets the effect of the pars anterior predominates.—T C B

The HYPOPHYSIS following brain lesions (L'ipofisi nelle lesioni del cervello) Desogus (V), *Riforma med* (Napoli), 1922, **38**, 329-330

The author reports his observations on the hypophysis in experiments on dogs in which either both the cerebral hemispheres, or only the occipital or the parietal or the frontal lobe had been removed. The results were the same whichever part of the brain cortex was destroyed. In 20 to 30 days after the trauma, hyperfunction of the hypophysis was found with intense hyperemia, eosinophilia and secretion of pure eosinophil colloid (same as basophil in the parenchyma of the lobe). In 30 to 60 days the eosinophils began to fade while the "chief" cells became evident. The capillary vessels were full of colloid, causing the organ to appear almost like a thyroid. The glandular parenchyma showed lacunae as if it were disintegrating. Analogous appearance was shown by the nervous portion and by the paranervous lobe, still basophil. From the 60th to the 90th day, eosinophils and basophils almost disappeared, while the chief cells were more evident than ever. The colloid became almost mother-of-pearl in color and was very abundant to the extent of breaking the capillaries and forming real colloid lakes. When the colloids had been absorbed the hypophysis showed a condition of absolute rest. After the 100th day there was a functional reintegration of the gland. The author recalls analogous results obtained by Ceni in the thyroid and suprarenal and the opposed results also obtained by Ceni in the male and female sexual gland. From this he infers the existence of a special visceral center on the brain cortex, connected with the function of the sexual and endocrine glands. The genetic centers have an exciting function. From the aforesaid, one can deduce that in dogs from one to two years old in which the animal regains normal condition after a brain cortex lesion in a period from 20 to 100 days, the hypophysis undergoes the following changes: hyperemia, secretion, hypersecretion, colloid resorption, rest of the organ and functional reactivation.—G V

(HYPOPHYSIS) Dystrophia adiposo-genitalis with muscular atrophy (Dystrophia adiposo-genitalis mit Muskelschwund) Fränkel (F),

Deutsche med Wchnschr (Berl), 1922, 48, 373, Klin Wchnschr (Berl), 1922, 1, 549

Demonstration of a patient who had been unable to walk since he was 8 years of age, and who always was extremely fat. He was 150 cm in height and 100 kg in weight. The hair was poorly developed, the generative organs were small, there was pseudoatrophy of the calves and atrophy of the glutei. His carbohydrate tolerance was low. The combination of dystrophia musculorum and hypoplasia of the hypophysis is not at all rare. It is probable that the endocrine organs have an influence in these diseases of the muscles

—J K

Tumor of the HYPOPHYSIS improved by x-rays (Durch Röntgenbestrahlung gebesserter Fall von Hypophysistumor) von Gerlőczy (G), Klin Wchnschr (Berl), 1922, 1, 1187

A short note. The symptoms included almost complete amaurosis, large sella, cessation of menstruation, headache, vomiting and giddiness. After x-ray treatment the eyesight was markedly improved and the symptoms of high intracranial pressure disappeared. In a case of hypophyseal infantilism x-ray treatment caused hypophyseal cachexia —J K

Tumor of the HYPOPHYSIS Goerke & Freund, Klin Wchnschr (Berl), 1922, 1, 297

A man of 69 had had a loss of physical and intellectual forces for 3 years. The only symptoms of a tumor of the hypophysis were the bitemporal hemianopsia and a typical radiogram. He was given surgical treatment, but it is not told whether this was successful

—J K

Influence of HYPOPHYSIS extracts on the alimentary tract and the blood of men (Einfluss von Hypophysenextrakten auf den Magen-Darmtraktus und das Blut des Menschen) Gorke (H) & Deloch (E), Arch f Verdauungskr (Berl), 1922, 29, 149-163

Subcutaneous injections of extract of neuro-hypophysis has the following effects. Secretion of salivary glands, pancreas and bile is diminished, but the ferment—or the bilirubin and cholesterol content is increased. The quantity of stomach content is generally increased, the acidity and the ferment content is diminished. Many persons show an increased tonus and peristalsis of the stomach and bowels. A few patients show an increased secretion of salt, bile and pancreatic juice and a low secretion of the stomach. Persons with an irritable nervous system show very strong reactions. In the blood a relative and absolute rise of leucocytes is seen. This is never very marked, however. The blood sugar does not show important changes —J K.

Tumor of the HYPOPHYSIS cured by radium (Ein Fall von Hypophysentumor geheilt durch Radium) Hirsch, Wien klin Wchnschr, 1922, 35, 402, Klin Wchnschr (Berl), 1922, 1, 1237

A short note The optical symptoms disappeared very soon
—J K

Characteristic effects upon growth, oestrus and ovulation induced by the intraperitoneal administration of fresh anterior HYPOPHYSEAL substance Evans (H M) & Long (J A), Proc Nat Acad Sc (Balt), 1922, 8, 38-39

The authors have shown that rats treated intraperitoneally with fresh extracts of beef hypophysis (anterior lobe), show an acceleration of growth which is in marked contrast to the lack of effects from oral administration. In this paper they report two series of experiments with litter mate controls which have been under observation more than a year. The animals are invariably heavier than the controls. In one case a rat having received hypophyseal extract weighed 596 grams on the 333rd day of life, while its healthy litter mate control weighed 248 grams. There was a large deposition of fat, but also an increase in the size and weight of the skeleton and of the viscera. The hypophysis, thyroid and thymus were not appreciably affected. Oestrus may never occur in these animals, or may be exhibited only at long intervals, and it was surprising to find the ovaries twice as heavy as those of the controls, and containing great numbers of corpora lutea. The uterus weighed only half as much as that of the controls. Histologically there was abundance of lutein tissue and normal graafian follicles. Extracts of the posterior lobe gave no such effects —T C B

Composition of the urine and of the blood of dogs deprived of the HYPOPHYSIS (Composition de l'urine et du sang des chiens privés d'hypophyse) Houssay (B A) & Mazzocco (P), Compt rend Soc de biol (Par), 1922, 86, 409-410

Adult dogs were kept in metabolism cages and the observations extended over a month for each dog. Some had total extirpation of the hypophysis, some were operated upon without disturbing the gland, some had a fragment of gauze left behind the hypophysis, and finally some were kept as normal controls. The results show that the blood and urine are normal in dogs deprived of the hypophysis. Tables are given —T C B

(HYPOPHYSIS) Endocrinology of dystrophia adiposo-genitalis Kanal (T), Nisshin Igaku, 1922, 11, (No 5), Jap Med World (Tokyo), 1922, 2, 166

The case was diagnosed by clinical symptoms. Pituitrin or pilocarpin gave negative results. According to the classifications of Eppinger and Hess it belonged to the sympathicotonic group.

Marked glycosuria was brought on by administration of 50 gms of glucose, or by giving adrenalin. Histidin prevented the glycosuria but cilosin and tryptophan had no controlling effect —R G B

Gas metabolism in diseases of the **HYPOPHYSIS** (*Gaswechseluntersuchungen bei Hypophysenerkrankungen*) Kestner, München med Wchnschr, 1922, 69, 796, Klin Wchnschr (Berl), 1922, 1, 1280

In dystrophia adiposo-genitalis, metabolism and the intake of food are only very slightly increased. Low metabolism is found in hypophyseal nanism and in some cases of endogenous adiposity. Injections of extract of pars anterior causes the metabolism to rise —J K

The clinical pathology of the **HYPOPHYSIS** and the interbrain (*Beiträge zur klinischen Pathologie der Hypophyse und des Zwischenhirns*) Leschke (E), München med Wchnschr, 1922, 69, 796, Klin Wchnschr (Berl), 1922, 1, 1280

The greatest quantity of active principle of hypophysis is found in the pars intermedia. Uterus contraction and a decreased diuresis are caused by different amins, resembling, but not identical with, histamin. Extract of pars anterior has an influence on metabolism useful in treatment of cachexia. Degeneration of the hypophysis causes cachexia, but never dystrophia adiposogenitalis or diabetes insipidus. Localization of these last mentioned diseases is in the interbrain, which, in turn, is influenced by the hypophysis. The hypophysis and interbrain have a regulating influence on each other —J K

A case of **HYPOPHYSEAL** cachexia (*Ein Fall Simondsscher Krankheit*) Lichwitz, Klin Wchnschr (Berl), 1922, 1, 397-398, Deutsche med Wchnschr (Berl), 1922, 48, 500, München med Wchnschr, 1922, 69, 138

The disease began in an acute form, with diabetes insipidus, loss of flesh, loss of beard and other hair, sexual impotence, and hemianopsia. The skiagram of the sella showed enlargement with a calcium shadow. X-ray treatment and administration of hypophysis preparations had a splendid effect. The concentration power of the kidney for sodium chloride did not become normal, however —J K

Genital dystrophy of **HYPOPHYSEAL** origin (*Genitale Dystrophie hypophysären Ursprungs*) von Liebermann (L), Klin Wchnschr (Berl), 1922, 1, 604

A woman of 44 had a very small sella turcica, and a partial atrophy of the optic nerve. No other details are given —J K

(**HYPOPHYSIS**) Independence of pulmonary circulation McDowall (R J S), Brit Ass Report, 1921, 446

Pituitary extracts cause rise of pulmonary pressure (60 experiments, Sharpey Schafer's method), which has no relation to any changes in aortic pressure. Perfusion experiments with the surviving lung support the view of independence.

—Physiol Abst, 7, 34

(HYPOPHYSIS) *Dystrophia adiposo-genitalis* Meisner, Deutsche med Wchnschr (Berl), 1922, 48, 647, Klin Wchnschr (Berl), 1922, 1, 497

A girl of 15 years, 1.33 M in height and 41.3 kg in weight, was troubled with atrophy of the optic nerves and peripheral chorioretinitis. No bitemporal hemianopsia was apparent. The Wassermann test was negative. No other details are given.

—J K

The physiological assay of PITUITARY extracts Nelson (E E), J Pharmacol & Exper Therap (Balt), 1922, 19, 270-271

Ten commercial preparations of pituitary extracts were assayed. Some were ten times the strength of others. The pressor method is satisfactory for the comparison of a large number of preparations. The pressor activity, however, is not necessarily a measure of the oxytocic strength. The most satisfactory test for the latter is the virgin guinea-pig uterus. Histamine is unsatisfactory because it is unstable. Potassium chloride is unsatisfactory because the irritability of uteri toward pituitary extract and this does not vary in a parallel manner.—F A H

(HYPOPHYSIS) Use of PITUITRIN in inoperable cancer Norgate (J H), Brit J Surg (Bristol), 1922, 9, 495

During a severe outbreak of enteric fever in 1919, finding that pituitary extract (posterior infundibular) controlled the hemorrhage cases without any bad symptoms, Norgate tried it in a case of sudden and severe hemorrhage from an extensive epithelioma of the tongue with enlarged cervical glands, injecting 1 cc into the tongue muscle. All bleeding stopped at once, and there was no repetition of it. Weekly injections into the tongue were given for three months, and the patient made rapid improvement, put on flesh, and the cachexia disappeared. He continued nine months in the state, then a hard mass formed in his liver, the growth in the tongue remaining the same, the glands slightly enlarged, and he died very emaciated. The first injection was given May 12, 1919, and he died April 27, 1920. His melancholy and suicidal tendencies improved up to about a month before his death. Similar results were obtained in thirty-six other cases. No claim is made by Norgate that pituitary extract is a cure for cancer, for it only delays the growth by cutting off its blood supply for a limited time, but as a general tonic to the system, as a great antagonist to cachexia.

and its attendant distress of mind and body, and as an agent in producing a remission for a time of the "last sentence" its value is great—J Am M Ass, 78, 1760

(HYPOPHYSIS) *Operierter Hypophysistumor* Oehlecker, Deutsche med Wchnschr (Berl), 1922, 48, 407

A patient with dystrophia adiposo-genitalis suffered from severe headaches, disturbances of sight, vertigo, etc After the operation there was improvement which lasted for about three years

—J K

Tumor of the HYPOPHYSIS Oehlecker & Fahr, Klin Wchnschr (Berl), 1922, 1, 299, München med Wchnschr, 1922, 69, 29

The patient was a woman of 31 with dystrophia adiposo-genitalis and bitemporal hemianopsia A tumor was removed and she was cured for the time, but died two years later from recurrence The tumor showed the picture of hypophysis tissue No symptoms of hypophyseal cachexia had developed—J K

(HYPOPHYSIS) **GIGANTISM** with hemorrhagic osteomyelitis of a metacarpal bone Packard (M) & Barrie (G), J Am M Ass (Chicago), 1922, 78, 8-10

A case of so-called preadolescent hyperpituitarism in a boy of sixteen, presenting all the stigmas of gigantism, is reported because of a unique accompanying condition, a hemorrhagic osteomyelitis of a metacarpal bone The family history is not relevant The bone changes in perverted pituitary function are discussed briefly, and radiograms and measurements of this case are given The hemorrhagic osteomyelitis cannot be definitely aligned with the pituitary disturbance, but is considered suggestive in view of the findings of other workers—W M A

The variability of the action of HYPOPHYSIS extract (*Sur la variabilité d'action des extraits hypophysaires*) Parisot (J) & Mathieu (P), J de physiol et de path, gén (Par), 1920, 18, 1182-1193

Small and large doses have opposite effects on involuntary muscle in general, including heart and blood vessels The small doses cause excitation, the large doses inhibition Therapeutic doses are excitatory—Physiol Abst, 6, 73

The influence of PITUITRIN on blood-sugar (*Ueber den Einfluss des Pituitrins auf den Blutzucker*) Partos (A) & Katz-Klein (Freida), Ztschr f d ges exper Med (Berl), 1921, 25, 98-110

When pituitrin is subcutaneously injected into rabbits there is produced a hyperglycemia and an increase in the water content of the blood The point of attack of pituitrin is the periphery The drug

acts as a retardant to adrenin hyperglycemia only to small degree This is attributable in part to the alteration in the dry matter content of the blood Pituitrin does not inhibit the hyperglycemia produced by theo-bromine —F S H

The influence of the HYPOPHYSIS upon growth, pathogenesis of acromegaly and gigantism (Ueber die Wachstumfunktionen der Hypophyse Die Pathogenese der Akromegalie und des Gigantismus) Petényi (G), Fortschr d Med (Leipz), 1922, 40, 213-217

Before the epiphyses are closed two kinds of growth disturbances may develop (1) acromegaly without increase in length growth, (2) hypophyseal gigantism without symptoms of acromegaly This makes it probable that the influence of the pars anterior of the hypophysis in bone growth is complicated There probably exists an influence on the enchondral growth and, independent of this, an influence on periosteal growth Both functions may undergo separate pathological changes Increased periosteal growth produces acromegaly, increased enchondral growth, gigantism If both functions are increased a mixed form develops

—J K

HYPOPHYSIS in acute infectious diseases (Hypophysenbefunde bei akuten Infektionskrankheiten) Plaut (A), Klin Wchnschr (Berl), 1922, 1, 552

Out of 35 cases of pyemia the hypophysis was affected 17 times The changes in the posterior lobe were generally inflammations, in the anterior lobe necrosis Acute meningitis rarely affects the hypophysis In influenza and diphtheria no changes were found in the hypophysis —J K

Respiratory metabolism in diseases of the HYPOPHYSIS (Gaswechsel bei Hypophysiserkrankungen) Plaut (R), Klin Wchnschr (Berl), 1922, 1, 552

A meal of 200 gms meat, 50 gm fat and 200 gm bread causes an originally normal basal metabolism to rise 25 to 35% In diseases of the hypophysis this rise is only $\pm 11\%$ Cases of adiposity with the same metabolism are probably of hypophyseal origin —J K

X-ray treatment of the HYPOPHYSIS and HYPOPHYSEAL infantilism (Hypophysenbestrahlung und hypophysärer Infantilismus) Poos (F), Klin Wchnschr (Berl), 1922, 1, 836-840

Fränkel and Geller have exposed the hypophysis of young female rabbits to x-rays and have observed that the generative organs remained small They concluded from this that x-rays influenced the generative organs via the hypophysis Poos has carried out the same experiments with the same results When, however, a leg,

for instance, is exposed to x-rays the effects are the same. When any organ is exposed to x-rays there is always a pathological change in all radiosensitive organs —J K

(HYPOPHYSIS) Malformations of the pars nervosa and infundibulum (*Gewebsmisbildungen in der Neurohypophyse und am Infundibulum*) Priesel (A), *Wien klin Wchnschr*, 1922, 35, 285

The author observed little nodules of large cells with much protoplasm in the neurohypophysis and in the infundibulum. The cells were epithelial-like, polygonal with indistinct walls, from time to time they showed other forms. The nodules were small, though they might reach the size of a pin head. Once a tumor the size of a pea was found. It is probable that these nodules were congenital malformations —J K

HYPOPHYSEAL dwarfism (*Ein Beitrag zur Kenntnis des hypophysären Zwergwuchses*) Priesel (A), *Beitr z path Anat u z allg Path* (Jena), 1920, 67, 220-274

A man 91 years of age, 132 cm tall, of good intelligence, never married. Autopsy showed developmental defects and tumor of the epithelial lobe and persistent cranio-pharyngeal canal. The skeleton is described. A careful histological study was made of the other endocrine organs also —W J A

Stimulative radiation of the HYPOPHYSIS (*Reizbestrahlung der Hypophyse*) Rahm, *Klin Wchnschr* (Berl), 1922, 1, 755

A short note. This treatment in young rabbits increases weight —J K

The casuistics of tumors of the HYPOPHYSIS (*Beitrag zur Kasuistik der Hypophysentumoren*) Roth (H), *Beitr z path, Anat u z allg Path* (Jena), 1920, 67, 309-328

Description of a case, including clinical, gross and microscopic findings —W J A

Cachexia and tuberculosis of the HYPOPHYSIS (*Kachexie bei Hypophysentuberkulose*) Schneider (H), *Klin Wchnschr* (Berl), 1922, 1, 1027

A girl of 18 suffered with osteomyelitis, after which she became cachectic, with slight symptoms of thyroid insufficiency. She had infantile sexual organs. The radiogram showed a small sella turcica. The tuberculin reaction was positive and a roentgenogram of the lungs showed enlarged glands. Her case was diagnosed as tuberculosis of the sella turcica and hypophysis. Organotherapy was not successful —J K

PITUITRIN Selhorst (J F), *Vox med* (Utrecht), 1922, 22, 51-53

An answer to Kouwer (see *Endocrinol*, 1922, 6, 156) defending pituitrin It is an extremely useful substance in obstetrics

—J K

Secretory processes in the **HYPOPHYSIS** (*Contribution à l'étude des processus de sécrétion dans l'hypophyse*) Stewart (F W), *Arch de Morph gén et expér (Par)*, 1922, 1, 46

Castration in the rabbit does not produce any change in the structure of the anterior lobe of the hypophysis The author states that many methods for staining the sections of the hypophysis are defective In the sinus and the intercellular spaces of the anterior lobe, cells are found, derived from the blood preparing organs They are formed partly by the connective tissue of the sella turcica A very large number of these cells is found in this connective tissue and in its vessels It is sometimes possible to see in the sections how these cells are digested—by phagocytosis by the cells of the hypophysis These cells play no role in the hypophysis The cells of the anterior part of the hypophysis are all of the same sort The cells are first basophilic and gradually become eosinophilic Often eosinophil granulations are found in the intercellular spaces The last stage of the cell is when its border is formed by an eosinophil ring, this ring gradually disappears, the cytoplasm becomes once more basophilic, and a new cycle of secretory activity begins Pycnosis of nuclei generally is a symptom of degeneration However, it may indicate also exhausted cells In this case, after some rest, the cell and the nucleus regain their normal appearance.

—J K

Oxytocic substances in posterior lobe of the **HYPOPHYSIS** (*Ueber den Gehalt der Hypophysenhinterlappen—Extrakte an uterusregenden Substanzen*) Trendelenburg (P), *Munchen med Wchnschr*, 1922, 69, 106-107

Comparison of some commercial preparations —J K

A case of **HYPOPHYSEAL** nanism (*Über einen Fall von hypophysärem Zwergwuchs*) Witthauer (W), *Klin Wchnschr (Berl)*, 1922, 1, 998

The author describes a man of 24 years, 136 cm in height, who had ceased to grow when he was 6 years old He never perspired, he was quite normally proportioned, he had no pubic or axillary hairs, his voice was infantile, diabetes was not manifest and he was very intelligent Radiograms showed a very large sella turcica and open epiphyses of all bones His carbohydrate tolerance was high Injection of adrenalin had almost no influence on the blood pressure and did not produce glucosuria Abderhalden's reaction was positive with testicle, adrenal and hypophysis The disease is probably caused by hypofunction of the pars anterior of the hypophysis —J K

Ergot, quinin and PITUITRIN Wright (A H), Canad M Ass J (Montreal), 1922, vii, 383-386

Of no endocrine interest—J H

Action of INTESTINAL extract and extracts of other organs on the bronchial musculature and the pulmonary circulation Hal-lion (L), Arch internat de physiol (Liège & Par), 1921, 18, 358-368

Extracts of intestinal mucosa exert a broncho-constrictor effect, and varied but characteristic responses in the circulation With the exception of renal extracts the results with extracts of other organs were found to be quite comparable—Chem Abst

LIPODYSTROPHIA progressiva Reuben (M S) & Zamkin (H O), Arch Pediat (N Y), 1922, 30, 112-116

Report of two cases in girls of 10 and 12 years of age with no symptoms referable to glands of internal secretion X-ray examination of both skulls were negative A short bibliography on the subject is appended—M B G

MONGOLIAN IDIOCY in one of twins McLean (S), J Am M Ass (Chicago), 1922, 78, 13-15

A mongolian idiot with a normal twin sister is evidence against any endocrine disturbance or general condition in the mother being an etiological factor The author suggests that in this case an abnormality in one of a pair of germ cells may be responsible A brief reference is made to the interest of endocrinologists in mongolian idiocy—W M A

Notes on MONGOLISM Thursfield (H), Brit J Child Dis (Lond), 1921, 18, 18-21

Basing his studies upon 42 mongolian idiots which he was able to observe for a number of years, Thursfield concludes that there is no proof that the mongolian is the last of a long family or that he is born at the end of the child bearing period Health during pregnancy and the difficulty of the labor had no influence on the production of mongolianism The incidence of previous miscarriages in the mother was also small as only 19 of the 42 gave such a history Tuberculosis and syphilis and other infectious diseases apparently do not play much of an etiological role, but prevention of conception or measures at attempts may have some bearing He found that 7 of the 42 mongolians had cardiac defects Incurving of the last phalanx of the little finger was found in 13, absent in 16 and not noted in 13 The fissured tongue was not present in the first few months of a child's life, at least not before 12 months In the author's experience, speech, general in-

telligence, obedience and even temper seemed to be promoted by the use of thyroid extract. Mentality was not so amenable to treatment—M B G

ORGANOTHERAPY (Über Organotherapie) Biedl (A), *Ztschr f ärztl Fortbild (Jena)*, 1922, 19, 161-167

An admirably conservative lecture delivered by the author before a medical gathering in Berlin. The best example of logical and intelligent organotherapy is the administration of thyroid in cretinism and myxedema. Kocher has stated that after complete thyroidectomy the patient remains perfectly healthy if he receives thyroid preparations regularly. The author, however, believes that though this treatment is exceedingly useful, it is not completely adequate. Since we do not know any good way of standardizing thyroid preparations exact dosage is nearly impossible. Perhaps Kendall's thyroxin will prove of great use in avoiding this difficulty. As nearly all endocrine diseases are pluriglandular, organotherapy is very complicated and often is less successful than would be expected. To have success with organotherapy an exact study of the patient, of his "endocrine constellation" is necessary. A complete study of metabolism is also necessary in most cases, sometimes regular weighing of the patient is enough, but often an exact study of basal metabolism is needed. The author warns against our speaking of hyper- or hypo-function of an organ. As we do not know how to calculate the normal function of such a gland, these words indicate merely lack of physiological knowledge.

—J K

Division of work in the OVARY (Die Arbeitsteilung im Eiserstock). Guggisberg (H), *Zentralbl f Gynäk (Leipz)*, 1922, 46, 402-407

The ovary has at least three functions. It produces ova, it produces hormones influencing the secondary sex characteristics, and influences metabolism,—especially carbohydrate metabolism. When castrated rabbits are injected with 0.05 mg adrenalin the blood sugar increases, but when the animal is not castrated this reaction is not seen. The same results are seen after castration by radiation as by surgery. The animals become fat. The author has castrated the animals with x-rays and has examined the ovary some time afterwards. Changes in the interstitial cells were never seen. The follicles were severely degenerated. Therefore, he believes that the follicles have an influence on metabolism, if they degenerate, a change in metabolism occurs. Therefore it is believed that the follicles have an incretion and that the endocrine as well as external function of the ovary is due to the same elements.

—J K

Treatment of symptoms caused by loss of OVARY (Zur Therapie der ovariellen Ausfallserscheinungen) Halban (J), Klin Wchnschr (Berl), 1922, 1, 708

Loss of the endocrine function of the ovary causes a hypersensibility of the sympathetic. Organotherapy is not successful, but calcium, theobromin, and nitroglycerin are useful.—J K

Treatment of skin diseases of the menopause with OVARY (Ovarialtherapie klimakterischer Toxikodermien) Hofbauer (J), Zentralbl f Gynäk (Leipz), 1922, 46, 558-560

Report of two cases of skin diseases (no exact diagnosis is given), cured by injections of ovoglandol. Liuthlen in Vienna has reported good results from injections of ovoglandol or thyroid and hypophysis extract in pruritus vulvae and pruritus universalis, acne rosacea, chronic eczema and dermatitis bullosa faciei. That the ovaries have a relation to the skin is proved by the cases of dermatitis symmetrica dysmenorrhoeica.—J K

True diffuse PANCREAS hyperplasia (Echte diffuse Pankreashyperplasie) Sklawunos (T G), Centralbl f allg Path u path Anat (Jena), 1922, 32, 260-264

Sklawunos refers to the infrequency of hypertrophy of the pancreas and points out that the great majority of the cases have been seen in acromegaly. A case is reported which was not associated with this disease. The patient was a male, 58 years old, 170 cm in height and 64 kg in weight. He died of luetic aortitis, erysipelas and sepsis. The pancreas, stripped of all adventitial tissue, weighed 182 gms (normal average 83.5 gms), and measured 25x6.5x3 cm (normal average equals 18.4x5x2.5 cm). The weight and dimensions were therefore at the upper border of physiological variation and in relation to body weight it was 0.28% as compared with the normal of 0.15%. The author states that there was a true hyperplasia of the gland tubules giving a relative decrease in the number of islands of Langerhans irrespective of the portion of the pancreas studied. He was unable to find a cause for the enlargement, as all the bile ducts, pancreatic ducts and intestinal mucosa were normal. There was a gastric ulcer which he thinks was of no significance. He refers to the possibility of congenital hypertrophy similar to that seen in the spleen, thyroid, mammary glands, etc., and also discusses the possibility of its being an acquired compensatory hyperplasia due to some deficiency of digestive enzymes.—D M

PARATHYROID transplantation (Epithelkörperchentransplantation) Eden, Klin Wchnschr (Berl), 1922, 1, 1022

A short note. Transplantation is recommended in cases of postoperative tetany.—J K

(PARATHYROID) The tetany syndrome and its pathogenesis (Das Tetaniesyndrom und seine Pathogenese) Frank (E), Klin Wchnschr (Berl), 1922, 1, 305-309

A general review without new facts —J K

(PARATHYROID) Studies on the pathogenesis of infantile tetany (Untersuchungen über die Pathogenese der infantilen Tetanie) Freudenberg (E) & Gvorgy (P), Klin Wchnschr (Berl), 1922, 1, 222

Will be published in detail in Jahrb f Kinderh —J K

(PARATHYROID) Severe tetany (Schwere Tetanie) Hohlbaum, Klin Wchnschr (Berl), 1922, 1, 399, München med Wchnschr, 1922, 69, 332

In a nurse of 22, suffering from severe tetany, the parathyroids were grafted from a woman who had just died. The day after the operation there was a slight attack, then for 3 weeks, no attacks, increase of electrical irritability disappeared. Only the Chvostek symptoms were still positive —J K

(PARATHYROID) Postoperative tetany and coma parathyreoprivum Mann (L) Zentralbl f Chir (Leipz), 1922, 40, 548-549

Administration of thyroid tablets in two cases of postoperative tetany caused one patient for 3 years, the other for 4 years to be free or nearly free from attacks. A third patient in whom strumectomy was performed with ligation of the 4 arteries fell into a coma resembling that of encephalitis. The tendon jerks were negative. Trousseau's symptom was slightly positive. Cure was effected by administration of thyroid (doses not given) —J K

(PARATHYROID) Tetany and hypertrophic cirrhosis of the liver (Tetanie bei hypertrophischer Lebercirrhose) Schur (N), Klin Wchnschr (Berl), 1922, 1, 1028, Wien klin Wchnschr, 1922, 35, 491

The patient suffered from Hanot's cirrhosis and had typical attacks of tetany. This was probably due to parathyroid insufficiency. She had the same attacks when she fed a child —J K

The pathology of the PINEAL gland. Epiphyseal adiposity with tumor-like degeneration of the organ (Zur Pathologie der Zirbeldrüse. Epiphysäre Fettsucht bei geschwulstförmiger Entartung des Organs) Lowenthal (K), Beitr z path Anat u z allg Path (Jena), 1920, 67, 207-219

A man of 23 years developed a pineal gland tumor the local symptoms of which were preceded for a considerable period by clinical manifestations including adiposity. The tumor had an epi-

thelial structure and clearly resembled the functioning (?) pineal of the newborn. It is held that hyperactivity of the pineal is responsible for epiphyseal adiposity—W J A

Secretin studies (Sekretinstudien, I, II) Eweyk (C van) & Tenenbaum (M), Biochem Ztschr (Berl), 1921, 126, 238-245

Protein (casein) materials, after heating to 150-70°C, become secretin-containing, in the sense that they will cause the secretion of gastric juice in the Pawlow dog. This effect is due to the presence of histamine. It had been shown previously by Popielski that histamine would act as this type of secretin. The hormone from spinach is not histamine—Med Sc, 6, 155

The action of SECRETIN (L'action de la sécrétine) Halliburton (W D) & de Souza (D H), Arch internat de physiol (Liège & Par), 1921, 18, 231-241, abst Physiol Abst, 7, 52

In the preparation of secretin a boiling temperature is advantageous in that the coagulable proteins are eliminated, but one can very well operate at a low temperature. False secretin, an extract of spinach, or that which produces hydrolysed proteins, is not deserving of the name,—it is only slightly active and plays no role in digestion. Secretin injected by portal vein is less active than that injected by jugular vein, probably because in the first case there is more dilution in the blood—F A H

(SPLEEN) Pathology of polycythemia (Zur Pathologie der Erythraemie) Brieger (H) & Forschbach (J), Klin Wchnschr (Berl), 1922, 1, 845-848

In polycythemia the number of leucocytes and platelets as well as the red cells may be increased. In some cases, the patient with polycythemia dies with all symptoms of leukemia. When the spleen is removed the number of red corpuscles is temporarily increased. A case is reported in which this operation was followed by polycythemia and a very large number of leucocytes. It is probable that the spleen controls the action of the bone marrow. Polycythemia is also seen in cases of endocrine disturbances, especially in **dysthyroidism**. This kind of polycythemia, however, differs from the cases mentioned above in that there is generally leukopenia with lymphocytosis—J K

The relation of SPLENECTOMY to growth and appetite in the rat Smith (A H) & Ascham (Leah), Am J Physiol (Balt), 1922, 60, 250-254

It has been repeatedly asserted that increased appetite and decreased activity result from removal of the spleen. The observations have been made usually without regard to accurate measurements or careful control of conditions. The authors used rats,

splenectomized at the age of 40 days The controls were subjected to the traumatism of the operation without removal of the spleen Osborne and Mendel's diet was given with the addition of 0.4 gm dried brewery yeast to supply vitamine B The observations extended over 43 weeks The authors concluded that there is no evidence of increased appetite, no anaemia nor any departure from the normal rate of growth —T C B

Function of the SPLEEN under physiological and pathological conditions (Über die Funktion der Milz unter physiologischen Verhältnissen) Weicksel (J), Ztschr f klin Med (Berl), 1922, 94, 90-100

Of no endocrine interest —J K

A case of TETANY after gastro-enterostomy (Auftreten von Tetanie im Anschluß an eine Gastroenterostomie) Baumann (M), Zentralbl f Chir (Leipz), 1922, 49, 250-253

Three days after a gastro-enterostomy for a stenosis of the pylorus typical tetany attack occurred, followed by another attack 10 days later After this, no attacks were observed Whether the parathyroids were factors is not known —J K

Pathogenetic relations between TETANY and rickets (Pathogenetischen Beziehungen zwischen Tetanie und Rachitis) Freudenberg (E) & Gyorgy (G), München med Wchnschr, 1922, 69, 422

The authors believe that symptoms of rickets always exist in tetany The calcium content of the blood in rickets is normal, the phosphates are decreased In manifest tetany the calcium is always low, the phosphates, normal or slightly increased In the urine in rickets the quantity of phosphates and ammonia is high (acidosis), in tetany it is low (alkalosis) So there is a real contrast between rickets and tetany When a patient with rickets gets tetany, it means that his acidosis is changed into alkalosis The authors believe that this change can be accomplished by hormones This is made probable by the fact that tetany generally begins or increases in spring, the season in which other endocrine conditioned processes, e g, growth, are most intense These facts are of importance for the treatment of tetany All drugs or other treatments producing acidosis may be useful NH_4Cl produces a rise in the excretion of phosphates, a phosphate diuresis with a calcium retention Ingestion of acids and starvation tend to cure tetany —J K

Spasmophilia and TETANY (Krampfbereitschaft und Tetanie) Gott (T), Klin Wchnschr (Berl), 1922, 1, 553, München, med Wchnschr, 1922, 69, 688

Not of endocrine origin —J K

Postoperative TETANY after goiter operations (Postoperative Tetanie nach Kropfoperationen) Knaus (H), Beitr z klin Chir (Tübing), 1922, 125, 669-680

In 619 operations for goiter 5 cases of tetany were seen Two ended fatally Three cases were seen after operation for a recurrent goiter Knaus examined the removed piece of thyroid histologically Parathyroids had been removed 21 times No symptoms of tetany developed except in one case—J K

Epilepsy in postoperative TETANY (Epilepsie bei postoperativer Tetanie) Koetzle (H), Zentralbl f Chir (Leipz), 1922, 49, 365-368

A man of 20 underwent hemistrumectomy Two years later a hemistrumectomy was performed on the other side Three days after this operation tetany set in, followed by epileptic fits Epilepsy has occurred in a few former cases after goiter operation There is an interesting relation between epilepsy and the endocrine organs —J K

Two cases of postoperative TETANY after removal of the THYROID (Zwei Fälle von postoperativer Tetanie nach Schilddrusenexstirpation) Mann, Klin Wchnschr (Berl), 1922, 1, 550

A short note without details In one case of resection of the thyroid with ligation of the 4 arteries the patient fell into coma parathyreopriva—J K

Relations between the chemistry of the body and TETANY (Beziehungen des Chemismus des Organismus zur Tetanie) Orgler (A), Klin Wchnschr (Berl), 1922, 1, 1023, München med Wchnschr, 1922, 60, 451

Tetany of infants largely depends on the food Potassium and phosphorus increase the symptoms, calcium and magnesium have a good influence In many cases the calcium balance is negative The calcium content of the blood is low Parathyroid tetany, guanidin tetany and spontaneous tetany of infants all show the same type of calcium metabolism—J K

Serious TETANY after severe enteritis (Schwere tetanische Erscheinungen bei heftiger Enteritis) Severin, Klin Wchnschr (Berl), 1922, 1, 550

In \pm 10 cases the author observed tetany after enteritis and in one case after ileus In these cases the tetany is latent—J K

Anatomy of the THYMUS in rabbits of different ages (Zur Altersanatomie der Kaninchenthymus) Gedda (E), Upsala Läkaref Förh, 1921, 26, 1-27, J Aug Hammer, Festschrift Each article is paged separately

The author has made an examination of the thymus gland from 124 rabbits of different ages. Most of the endocrine glands and the lymphoid tissue of the same animals were before numerically examined by Hellman and others. The curve indicating the weight of the thymus gland as a whole showed a considerable difference from the values noted by Soderlund and Backman in their early investigation, but those demonstrating the weight of the parenchyma showed a most remarkable resemblance. Hence, the difference in weight is due to the fat component and not to the parenchyma. The relation between the cortex and the medulla is not altered at different ages. Thus the thymus of the rabbit differs from the human thymus, showing a comparatively greater involution of the cortex. Probably this phenomenon is due to the general greater importance of the lymphocytes in the rabbit during all ages of life, proving that Hammar is right in asserting that the changes of the lymphocytes in the thymus gland are conditioned not by local but by general factors.

—H B

Microscopical analysis of the THYMUS in certain cases of congenital syphilis (Beitrage zur Konstitutionsanatomie VII. Mikroskopische Analyse der Thymus in einigen Fallen von Lues congenita). Hammar (J A), Beitr z path Anat u z allg Path (Jena), 1920, 66, 37-81, 195-258.

An exhaustive review of the literature on the subject is given. A careful quantitative analysis is made of the thymus in a large number of cases of congenital lues. Percentages of volume are given for the cortex, the medulla and the Hassall's corpuscles, and these are compared with the normal percentages.—W J A

Reaction of the THYMUS in acute infections Microscopic analysis of the thymus in 21 cases of diphtheria (Verhalten der Thymus bei akuten Infektionen. Mikroskopische Analyse der Thymus in 21 Fallen von Diphtherie). Hammar (J A) & Lagergren (K A), Ztschr f ang Anat [etc] (Berl), 1918, 3, 314-398.

The detailed data of an elaborate quantitative analysis of the thymus in 21 cases of diphtheria are given. In all of these cases except one, the whole organ and the parenchyma were below the average. The smaller Hassall's corpuscles were, on the contrary, strikingly increased. The interstitial tissue in 3 cases was above normal, in 10 cases within normal limits and in the other 8 cases below normal.—A. T R

La radiotherapie de la maladie de Basedow et des autres formes de l'hyperthyroidisme Alschek (E), These de Paris, 1920, 56 p.

This thesis reports 5 cases of exophthalmic goiter in which the x-ray treatment, using the Bécclère technique, is stated to have brought about cure. The observations were made in the service of Dr Bécclère.—E G

(**THYROID**) Exophthalmic goiter and hyperthyreotoxic adenoma as two independent diseases (*Der exophthalmische Kropf und das hyperthyreotoxische Adenom als zwei selbständige Krankheiten*) Bircher (M E), Schweiz med Wchnschr (Basel), 1922, 52, 347

The writer—a Fellow in Medicine at the Mayo Clinic—summarizes the views concerning the nature and treatment of exophthalmic goiter presumably held by the staff of the Mayo Clinic. He outlines the several steps carried out in that clinic in the diagnosis, classifications, treatment and prognosis. Bircher states that more goiter cases are seen at the Mayo Clinic in two years than the late Professor T. Kocher saw in his entire lifetime and concludes the review by observing that it is remarkable that such high grade scientific work is being done in a country which half a century ago was a wilderness.—D M

(**THYROID**) Goiter prophylaxis (*Zur Frage der Kropfprophylaxe*) Bleyer, München med Wchnschr, 1922, 69, 587-589

The author first gives a short review of the geographical distribution of goiter in Bavaria and Switzerland. The increased number of goiter cases in Germany may perhaps be attributed to the fact that since the beginning of the war the importation of guano and artificial manure in Germany has ceased. The artificial mixtures that are now used are absolutely iodine free.—J K

(**THYROID**) Hereditary goiter (*Erblichkeitsfrage des Kropfes*) Bluhm (A), Arch f Rassen-u Gesellsch -Biol (Leipz), 1922, 14, 1

There is a theory that all goiters, the endemic forms included, are typically hereditary diseases. Another theory, given by Siemens, is that endemic goiter is not hereditary, but that sporadic goiter is. Bluhm gives the genealogical tree of a family for four generations. This family seems to confirm Siemens' theory. In studying these questions it is of great importance to examine the so-called healthy members of a family and to note minor changes in the thyroid also.—J K

Blood sugar after x-ray treatment of **THYROID** (*Das Verhalten des Blutzuckers nach Röntgenbestrahlung der Schilddrüse*) Brosamlen, München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1281

Small doses of x-rays on the thyroid produce an increase, larger doses a decrease of blood sugar. In Graves' disease these effects are more marked than in healthy persons.—J K

THYROID function from a chemical viewpoint. Cameron (A T), Canad M Ass J, 1922, 12, 229-232

A short account of our present knowledge of the chemistry of the normal and pathological thyroid in which the following points

are emphasized the thyroid elaborates iodothyroglobulin, as the storage form of thyroxin, the necessary tryptophane and iodide being normally present in blood. Administration of iodine compounds is useful only in so far as iodide is set free. Thyroxin is not toxic in itself, but when present in circulating blood in amounts greater than normal causes undue tissue destruction and cell starvation and so acts as an indirect poison. For prolonged administration by mouth, desiccated thyroid seems more suitable than thyroxin, although it is essential that the iodine content be stated, since its thyroxin effect will be approximately proportional to its iodine content —J H

(THYROID) The influence of war alimentation on Graves' disease (Sull' influenza dell' alimentazione di guerra sul morbo di Basedow) Curschmann (H), *Riforma med* (Napoli), 1922, **38**, 273-275

From personal and other doctors' observations the author concludes that the period of hypoalimentation during and after the war has had an undeniably good effect on patients with Basedow's disease. The numerous cases of myxedema, rather frequent during the years of famine, and the accentuation of hypothyroidism strengthens his point. As a consequence, the author would suggest that not meat only, but any kind of meal giving too many calories, might induce hyperfunction of the thyroid and therefore render the condition in the Basedow patients worse. He suggests thorough research work in this field —G V

The action of **THYROID** extract of a dog on the isolated heart of a normal or sensitized rabbit (Action de l'extrait thyroïdien de chien sur le coeur isolé du lapin normal ou du lapin sensibilisé) Demoor (J O), *Arch internat de physiol* (Liège & Par), 1921, **18**, 369-390, *Abst*, *Physiol Abst*, **7**, 50

The depressor action resulting from the addition of liquid thyroid extract of a dog to Locke's fluid perfused through the isolated heart of a rabbit is replaced by a pressor action if the rabbit has been previously sensitized by the intraperitoneal injection of thyroid extract. The author believes that immunity and anaphylaxis result from changes in the colloidal equilibrium of the blood or of the tissues —R G H

(THYROID) Serum concentration and viscosity of the blood in Graves' disease (Über die Serumkonzentration und die Viskosität des Blutes bei der Basedowschen Krankheit) Deusch (G) *Deutsches Arch f klin Med Leipzig*, 1922, **138**, 175-180

The viscosity of the total blood in Graves' disease does not show any typical change. In serious cases, however, the viscosity of the serum is decreased and its protein content, when tested with the refractometer, is low. The influence of treatment (operation, x-ray)

is seen by a rise of viscosity and a higher protein content of the serum When thyroïdin is given to healthy persons a lowering of viscosity and protein content of the serum may be found—J K

A plea for early diagnosis and treatment of HYPERTHYROIDISM
Dowden (C W) & Enfield (C D), Kentucky M J (Louisville), 1922, 20, 196

Treatment of hyperthyroidism, to be entirely satisfactory, must be instituted in the earlier stages of the disease, before organic damage has been wrought The bearing of the basal metabolic rate, the use of adrenalin (for observation of pulse, blood pressure and tremor), and the sugar tolerance test are discussed The adrenalin test the author does not regard as useful Vague and indefinite symptoms are also discussed It is asserted by the writer that no medical treatment of hyperthyroidism has as yet stood the test of time Surgery and roentgenotherapy are the only means of therapy that these writers regard as useful in this disease Crile's summary of the relative advantages and disadvantages of surgical and x-ray treatment are discussed A contrast is drawn between the period of incapacitation following surgery and the relatively very little time required for roentgenotherapy of this lesion While Crile shows a one per cent death rate in his statistics, x-ray statistics show absolute lack of mortality applied to this particular treatment Since many patients will not submit to surgical treatment, but will submit to x-ray in the early and curable stage of the disease, x-ray therefore could and does often prevent a fatal outcome in these particular cases Also the authors favor roentgenotherapy because of the fact that it attempts to restore the normal thyroxin balance without a mass attack If this attempt fails surgery is still an open recourse The technique employed by these authors is as follows The basal metabolism test, the Goetsch test and the sugar tolerance test are all made before x-ray is given Three areas are treated, one on the right over the thyroid going to the middle line, similarly one on the left, and a third one over the thymus region Eighty kv (about eight and one-half inch spark gap), five ma, twelve inches anode-skin distance, four mm aluminum and one cm of sole leather, ten to fifteen minutes exposure at intervals of a week or ten days Six such treatments are given unless the pulse drops rapidly after the first three or four treatments After a period of two to three weeks the metabolic rate is again taken If this is still high only a month's rest is given and a second series of similar treatments is then employed Otherwise, a three months' period is allowed to elapse and the basal metabolic rate is then again determined Complete cure, as far as symptoms and laboratory tests can determine has been accomplished in some cases and decided relief has resulted in others Case reports are appended—J Radiol, 1922, 3, 253

Direct continuity between PARATHYROID, THYROID and THYMUS
in mammals (Sur l'existence de rapports de continuité directe

entre parathyroides, thyroïdes et nodules thymiques chez les mammifères) Dustin (A P) & Gérard (P), *Compt rend Soc belge biol*, 1921, 85, 876-877

The authors describe the existence in the cat of connections between thymic tissue, thyroid tissue and parathyroid tissue This was formerly shown by Aimé and by Dustin in reptiles

—Physiol Abst

Relations between intestinal movements and the **THYROID** (Ueber die Beziehungen zwischen Schilddrüse und Darmbewegung) Deusch, München *med Wchnschr*, 1922, 69, 797, *Klin Wchnschr* (Berl), 1922, 1, 1281

In chronic constipation there is often hypothyroidism Administration of thyroid brings good results —J K

(**THYROID**) Exophthalmic GOITER Edmunds (W), A lecture delivered at the North-East London Post-Graduate College, April 27, 1921, London, 1921, 1-34

The loss of Ca which occurs both in Graves' disease and in diabetes, and the fact that Graves' disease is sometimes followed by diabetes, show that the two are related A cure should be sought in both cases by the administration of Ca, or possibly of Sr

—Physiol Abst, 7, 50

(**THYROID**) Radical operation for Graves' disease (Radikaloperation der Basedowstruma) Els, *Klin Wchnschr* (Berl), 1922, 1, 549

In extremely serious cases the author advises the complete removal of the thyroid and leaving a piece of gland the size of a cherry It is rarely necessary to give thyroïdin Els operated upon 4 patients without tetany following His results were very good

—J K

Treatment of chilblains and chronic freezing with **THYROID** preparations (Ueber Behandlung der Pernionen und der chronischen Erfrierungen mit Schilddrüsenpräparaten) Embden (H), München *med Wchnschr*, 1922, 69, 201

The author observed a patient with hypothyroidism who always suffered from chilblains Administration of thyroid tablets had a good effect on the chilblains as well as on the hypothyroidism He then tried this treatment in other patients with chilblains In some patients the effect was excellent, other cases were not improved It is not possible to tell beforehand in which cases treatment will give results —J K

(**THYROID**) Goiter (Über den Kropf) Enderlen, *Klin Wchnschr* (Berl), 1922, 1, 457-461

A general review without new data —J K

(**THYROID**) The Roentgen treatment of morbus basedowii Fischer (J F), *Acta Radiol*, 1921, 1, 179

In the beginning of his paper the author refers to the literature upon the subject of his paper, giving references. In all, he has treated 490 cases. 231 of these were private cases, of which a third were somewhat doubtful, a third slight, and a third severe cases of the disease. A case to illustrate the difficulty in diagnosis is given and discussed. Out of all the cases only 11 were of men. The majority of the patients were between 30 and 45 years, and the duration of the disease, for the most part, from 6 months to 5 years. Those treated at hospital and those treated privately were discussed separately as they are in different social positions, which is of importance. Those treated in hospital usually are laborers, and this increases the risk of contracting the disease. The method of treating private patients is given. Recurrence nearly always occurs in hospital cases, and the author states that this is due to overwork or domestic troubles. Taking the patients as a whole, four-fifths have benefited from the treatment and the remainder, even if no better, have not changed for the worse. Only one patient died. Patients in whom tachycardia predominates over the nervous symptoms are those in whom x-ray treatment is most likely to fail. Fourteen cases are then described with moderately full notes and in each case at least two photographs are given, one before and one after treatment. According to the author, improvement begins after the first series of irradiations. Weight should be observed, and in almost all cases where the patient is deriving benefit there is an increase in weight, often occurring about a month after the beginning of the treatment, though at first there may be a small loss. The effect of treatment on the various symptoms and the duration of benefit is related. Complications of x-ray treatment are next dealt with, particularly whether there is any danger to the patient, the author believes that there is none if treatment be carried out by skilled hands. The subjects which die are those in whom the disease is severe, and in them spontaneous hyperthyroidism may occur with no treatment, as is shown by a case quoted. It is not denied that in some circumstances x-rays may have an unfavorable effect. The author agrees with the vast majority that small doses are advisable in severe cases so as to avoid x-ray sickness, he quotes Nordentoft, who says that small doses would tend to cause hyperthyroidism, whereas large doses would not. The fact that the patient's skin is always very sensitive demands caution as a smaller dose than might be expected will often cause erythema. Various other possible complications are mentioned. The technique is then described. Author views the x-ray as far preferable to surgery, and says it should always be used unless there is a danger in putting off an operation which he considers to be a very rare event.—*Med Sc*, 6, 171-172

(**THYROID**) Technique of goiter operation (Technik und Methodik der Kropfoperationen) Florcken, Klin Wchnschr (Berl), 1922, 1, 876, München med Wchnschr, 1922, 69, 526

Of technical surgical interest —J K

Treatment of the remainder of the **THYROID** after operations for goiter (Zur Stumpfversorgung bei Kropfoperationen) Florcken (H), Zentralbl f Chir (Leipz), 1922, 49, 120

Of technical, surgical interest —J K

(**THYROID**) Frequency of goiter in school children in Munich (Kropfhäufigkeit bei Münchener Fortbildungsschulern) Fürst, München med Wchnschr, 1922, 69, 156

Krauter has shown that the number of girls with goiter in Munich has increased in the last years. In young individuals the author often observed a combination of underfeeding, goiter and hypogenitalism. He confirms the facts described by Krauter

—J K

The influence of **THYROIDIN** on blood viscosity and serum concentration in healthy persons (Ueber den Einfluss des Thyreoidins auf die Blutviscosität und Serumkonzentration bei Gesunden) Frowein (B), Ztschr f d ges exper Med (Berl), 1921, 24, 162-165

When 0.1 thyreodin is given 3 or 4 times a day for periods of 2 or 3 weeks to healthy individuals the concentration of the blood serum is decreased and the viscosity remains the same. The effect on the serum concentration was determined by changes in the refractive index —F S H

(**THYROID**) A case of formes frustes of Graves' disease and a case of premenstrual goiter (Ein Fall von Basedowoid und ein Fall von pramenstrueller Struma) Gottlieb (K), Wien klin Wchnschr, 1922, 35, 402

The author reports the case of a girl of 13 with nervous irritability, restlessness, gradually increased size of the neck, exophthalmos, perspiration, diarrhea and no menstruation. Graefe's symptom was positive in one eye. Another girl of 13 is also described who is restless and nervous and in whom a goiter is always seen before menstruation —J K

(**THYROID**) Treatment of endemic goiter (Behandlung des endemischen Kropfes) Grassl, München med Wchnschr, 1922, 69, 785

In Bavaria an old popular remedy for goiter is cod-liver oil. Its good effects are probably due to its iodine content —J K

Climatic treatment of **THYROID** diseases (*Klimabehandlung der Schilddrüsenerkrankungen*) Guhr, Deutsche med Wchnschr (Berl), 1922, 48, 544, Klin Wchnschr (Berl), 1922, 1, 970, Wien klin Wchnschr, 1922, 35, 533

A short note Patients with Graves' disease need a high mountainous climate—J K

(**THYROID**) Case of so-called metastasizing colloid goiter (*Zur Kasuistik der sog metastasierenden Kolloidstruma*) Guth (K), Zentralbl f allg Path u path Anat (Jena), 1922, 32, 257-260

Guth reports the pathological findings in the case of a woman, aged 39, who died of generalized tuberculosis originating in chronic pulmonary tuberculosis The thyroid gland was much enlarged, irregular in outline, and contained adenomata in both the lateral and median lobes Some of these adenomata were hemorrhagic, others grayish-white, others grayish-yellow on section Metastases were confined to a few nodules in the subperitoneal tissue in the region of the neck of the gall bladder Microscopic examination of these metastases showed well differentiated thyroid alveoli containing colloid and similar in appearance to some of the adenomas found in the thyroid gland He refers to Jaeger's four groups of metastasizing goiters, viz, (1) those in which the primary tumor and metastases are composed entirely of cancer tissue, (2) those in which the metastases showed both benign goiter tissue and cancer, (3) those in which it is difficult to determine what portion of the tumors are carcinomatous, and (4) those apparently benign goiters showing metastases with normal thyroid alveoli formations throughout He refers to the famous Cohnheim case of a metastasizing colloid goiter, but does not mention von Recklinghausen's pertinent criticism—D M

The role of the **THYROID** in heat regulation and fever metabolism (*Zur Rolle der Schilddrüse für die Warmeregulation und den Fieberstoffwechsel*) Grafe (E) & Redwitz (von E), Ztschr f physiol Chem (Berl u Leipz), 1922, 119, 125-138

Fasted dogs were thyroidectomized and studied by means of the respiration calorimeter, when kept at temperatures of 14°, 20° and 27° to 30° C The results of the investigation show that the loss of the thyroid did not seriously interfere with the chemical heat regulation of the organism Only in the very small animals did cooling produce effects One must, therefore, conclude that the thyroid is not as important a regulator of these processes as is generally believed In only one dog was fever induced The active agent was bac suipestifer Strange to say the dog lived The metabolism increased markedly during the course of the fever—F S H

(**THYROID**) The operative story of goiter Halsted (W S), Johns Hopkins Hosp Bull (Balt), 1920, 19, 71-257

The author gives a complete review of the history of the operative treatment of goiter. He sketches briefly his own interest in the subject and states that in 1879-1880, while he was working in Vienna upon the thyroid gland in the fish, he does not recall seeing a single operation for goiter in Billroth's clinic. From 1880 to 1886 he saw only one such operation in New York, when he assisted at an operation in which the patient was in the sitting posture with a rubber bag tied round his neck to collect the blood, and at the operation only two artery forceps were in use. The article is a monumental work which gives a complete review of the literature on the subject, and includes no less than 375 references. The story of the modern technique is very largely traced by means of extracts from the various papers. The earliest account of an operation upon the thyroid is apparently that of Albucasis, which was performed somewhere about the year 330. From this time there was practically no progress with the exception of a few rather doubtful reports in the fifteenth, sixteenth, and seventeenth centuries, until the eighteenth century. It is of interest to note that in 1596 an attempt was made to remove a goiter from a ten year old girl. She died under the operation and the surgeon was imprisoned. A case reported by Gooch in 1770 was followed by severe hemorrhage, which was controlled by compression day and night for eight days by persons alternating with each other at the task. In the first fifty years of the nineteenth century about a hundred cases are quoted, but the mortality was extremely high and the operation was strongly condemned by such surgeons as Robert Liston, J. Dieffenbach, and S. Gross. A quotation from the last of these three throws a most interesting light upon the progress which has been made in the last sixty years, although it is too long to reproduce here. In 1869, Billroth had performed the operation twenty times with eight deaths, and it was his work especially that gave the impetus to this branch of surgery. The severity of the operations as carried out in this period, when there was no anaesthesia, when arterial forceps were not yet discovered, and when the tumor had reached an enormous size before surgery was considered, is well shown by the full account which is given of the operation performed by Dupuytren. Long and careful extracts are given of most of the reported earlier operations, and in the accounts of them all it is easy to realize how extremely dangerous and difficult the operation was. Apparently somewhere between 1877 and 1880 forceps first began to be used, with an immediate improvement in the results, which have now reached such a stage of perfection that it is indeed difficult to realize that the great danger of this operation used to be the absolutely uncontrollable hemorrhage. In 1879 a series of successful cases by Billroth was reported, and included sixteen in the antiseptic series. Of a total number in which he performed the operation in the pre-antiseptic era thirteen out of thirty-six died, whereas in the antiseptic period there were only four deaths in forty-eight cases.

Kocher's work commenced in 1874, and he was the first to realize that complete removal of the thyroid was followed by the disastrous results that are so clearly recognized today. His papers, which are fully reviewed by Halsted, show the enormous progress that has been made, especially in the treatment of exophthalmic goiter, and in 1895 Kocher was able to review his first thousand cases of operations for goiter. Halsted then reviews the progress of his own work in America, and gives an account of his own operation which is now so well known. This portion of the work is the most brief of the whole, and from it one would hardly appreciate that Professor Halsted has practically lived through the whole period of modern progress in these operations, and has indeed done so much to produce the successful modern results. Although so brief an abstract is alone possible, the article is the most complete which has yet been published. A full account of the progress of this branch of surgery is given with very complete abstracts of every paper of note—*Med Sci*, 1922, 6, 37-38

(THYROID) Goiter in children (Kropf bei Kindern) Hamburger (F), *Wien klin Wchnschr*, 1922, 35, 470, *München med Wchnschr*, 1922, 69, 729, *Klin Wchnschr (Berl)*, 1922, 1, 1236

Goiter is not rare in children. It is nearly always a parenchymatous struma and often produces stridor. In infants it may produce symptoms of suffocation. As a child's neck is short, it is often difficult to feel the thyroid. In most cases 1 mg of NaI, three times a week is sufficient treatment—J K

The secretory action of the PANCREAS in relation to the THYROID gland I The effect of thyroid feeding in rats upon the secretory action of the pancreas Hashimoto (H), *Am J Physiol (Balt)*, 1922, 60, 357-364

A continuation of the work reported previously (*Endocrin*, 1920, 4, 56). Feeding large quantities of desiccated thyroid diminishes notably the amylase content of the pancreas. This may account for the digestive disturbances observed during thyroid feeding. On the contrary, small quantities cause a fair increase in function—T C B

The secretory action of the PANCREAS in relation to the THYROID gland II The effect of thyroidectomy in rats upon the secretory action of the pancreas Hashimoto (H), *Am J Physiol (Balt)*, 1922, 60, 365-370

Pursuing his studies further, the author finds that removal of the thyroid in rats results in a decrease in secretory activity of the pancreas. From all his observations Hashimoto concludes that the thyroid secretes an excitatory autacoid maintaining the normal functioning of the pancreas—T C B

(**THYROID**) Pathological changes in the heart in exophthalmic goiter Hashimoto (H), Iji Shimbun, 1922, No 1080, Jap Med World (Tokyo), 1922, 2, 75

The author produced interstitial myositis by feeding thyroid preparations He believes that there are similar changes in Basedow's disease In both they can be controlled and ameliorated by proper treatment See Endocrin , 5, 559 —R G B

(**THYROID**) The present day sources of common salt in relation to health, and especially to iodine scarcity and goiter Hayhurst (E R), J Am M Ass (Chicago), 1922, 78, 18-21

Many authors are quoted as to the distribution of iodine in nature, its scarcity in the present day dietary of man and animals, and the relation of this scarcity to goiter The last is not discussed except to emphasize the scarcity of goiter in maritime districts as compared with inland regions Iodine is present in very small quantities in the ordinary diet Commercial preparations of common salt contain no iodine even though the original source may have done so The methods of preparation remove all of it even when the salt is obtained from sea water The sea is the great store-house of iodine and the author therefore strongly recommends that sea water itself or a "salt" containing all the sea salts be used as a condiment This will furnish sufficient iodine as well as perhaps other valuable constituents —W M A

(**THYROID**) Light cases of hyperthyroidism (Die Hyperthyreosen leichteren Grades) Hellwig (A), Beitr z klin Chir (Tübing), 1922, 125, 75-116

An abbreviated version of the same article has been published in Deutsche med Wchnschr and previously abstracted —J K

Radium treatment of changes in the **THYROID** gland Heyerdahl (S A), Acta Radiol , 1921, 1, 207

Various authors are referred to who have used radium in preference to x-rays in treating thyroid lesions Aitkins, of Toronto, is quoted as saying that in acute cases radium must be supplemented by rest in bed, diet, and drugs Gamma rays alone are used Aitkins' technique and the opinions of Claquett, of Chicago, are mentioned The results of treating eight cases of plain goiter are given, in all the goiter was diminished and there was a change for the better The inconveniences of the treatment and the danger of telangiectasis are dealt with The author's opinion is that for this type of case radium will only be used when operation is out of the question The technique is described Eight cases of toxic goiter were treated, and the results and the effect of the treatment on symptoms are described Detailed notes of eight of the sixteen above mentioned cases are given and followed by those of four out of

eight cases of struma malignum, of which five showed temporary improvement and three no improvement—Med. Sci, 1922, 6, 85-86

Endocrinology and woman The **THYROID** and circulation (*Endocrinologie de la femme Thyroïde et circulation*) Ide (M), Rev méd de Louvain, 1921, 389-395

The author discusses the influence of the thyroid gland on the sexual function, the influence of the ovaries on the thyroid gland and the relations between the functions of the thyroid and circulation—R G H

(THYROID) Myxedema and Kaufmann's disease (*Myxödem und Kaufmannsche Krankheit*) Japha, Deutsche med Wchnschr (Berl), 1922, 48, 681-682

Demonstration of 3 patients with myxedema All were treated with thyroid, but only one, a girl of 25, developed enough to earn her living by needle work The two other patients are, though much improved, physically retarded Good results may be expected only when treatment begins as soon as possible A fourth case is also described, that of a girl of 9, closely resembling a case of myxedema She was suffering from micromegaly due to chondrodystrophy (Kaufmann's disease)—J K

(THYROID) X-ray findings in the trachea, especially after goiter operation (*Röntgenbefunde an der Trachea, besonders nach Kropfoperationen*) Kastner (H), Beitr z klin Chir (Tübing), 1921, 122, 455-474

When a goiter has reached a certain size its pressure may change the position and the form of the trachea The author found that after goiter operation the trachea quickly regained a position almost normal, and by a week after the operation its position was usually as nearly normal as it ever would be, an absolutely normal position often did not return This is not astonishing since a certain degree of tracheomalacia often exists The trachea often takes an abnormal place again some months or years after the operation This is probably due to the formation of cicatrix—J K

(THYROID) Goiter prophylaxis by means of iodine tablets (*Zur Kropfprophylaxe durch Iodtabletten*) Klinger (R), Schweiz med Wchnschr (Basel), 1922, 52, 315

The view seems to be spreading among medical men that sooner or later the prevention of simple goiter will be made general and automatic by the administration of iodine in table salt But for meeting the present condition in school children where both prevention and therapy are necessary, tablets certainly have a great value The author refers to "iodostarrin" tablets which he has used extensively during the last two years While probably one milligram

of iodine administered weekly is sufficient in most cases, four milligrams weekly can do no harm and is an additional safety —D M

(THYROID) Myxedema frustrum Kowitz, Klin Wchnschr, 1922, 1, 397, Deutsche med Wchnschr (Berl), 1922, 48, 472

No details are given The patient was a man of 51 years and after treatment with thyroid tablets metabolism became normal The excretion of water and salt, which had been defective before, became normal also —J K

Importance of gas metabolism determination for THYROIDIN treatment (Bedeutung des Stoffwechsels für die Thyroidintherapie) Kowitz, München med Wchnschr, 1922, 69, 796, Klin Wchnschr (Berl), 1922, 1, 1280

Merck's thyroid tablets increased metabolism always The effect is most marked in myxedema Patients with *dystrophia adiposo-genitalis* may show an increased sensitiveness to thyroidin —J K

(THYROID) The frequency of goiter in school children (Ueber die Verbreitung des Kropfes bei Schulkindern) Krauter (J), München Med Wchnschr, 1922, 69, 47-48

The prophylactic administration of small doses of iodine is recommended —J K

Compensatory hypertrophy of the THYROID gland Loeb (L), Tr Ass Am Physicians, 34 240-242

See Endocrin, 6, 357

(THYROID, HYPOPHYSIS) Dercum's disease (Dercumsche Krankheit) Loning, Klin Wchnschr (Berl), 1922, 1, 973

A short note The skiagram of the skull was negative Thyroid and hypophysis preparations were given without any success —J K

THYROID medication in certain nurslings of arrested development (La médication thyroïdienne chez certains nourrissons arrêtés dans leur développement) Maillet (M), Bull gén d therap [etc] (Par), 1922, 173, 214-216

Maillet reports his results from treating 32 poorly developed infants of 20 months of age with thyroid preparation The symptoms were apathy, hypotonicity, anorexia and vasomotor disturbances of the extremities From 1 to 2.5 ggm was the initial dose The effects had to be watched very closely Nervous conditions, insomnia and gastro-intestinal disturbances are contra-indications The changes in psychic condition and muscular tonicity are to be studied rather than the weight change in determining the effect of the drug The effects are observable in 8 to 15 days The following

doses are usually the same as the initial dose, although judgment must be made. The drug is given for 10 days, stopped for 10 days and so on —F S H

(THYROID) Surgical treatment of congenital goiter in an infant (Zur Operativen Behandlung der Struma congenita des Sauglings) Melchoir (E), Klin Wchnschr (Berl), 1922, 1, 472

Good results were obtained in a child of 7 months from an operation for cyanosis —J K

(THYROID) Pregnancy in sporadic cretinism (Schwangerschaft bei sporadischem Kretinismus) Merguet, Klin Wchnschr (Berl), 1922, 1, 971

A cretin of 28 years, who had not been treated, became pregnant. The child was born by cesarean section and died of unknown cause shortly after birth. The child appeared normal and had a histologically normal thyroid —J K

(THYROID) The goiter problem (Zur Kropffrage) Miesbach (E), Deutsche med Wchnschr (Berl), 1922, 48, 657-658

In all mountainous countries a long distance from the sea, but especially in the Alps, the kitchen salt, the water and the plants contain very little iodine. This is the case in Bavaria. There are in Bavaria some sources with large amounts of iodine, but these sources have no influence on the composition of the drinking water, hence here goiters may be attributed to low iodine content of the water. Kocher has shown that the goiters in fish disappear when iodine is added to the water. The work of Marine in Ohio and Klinger in Switzerland has proved the vital importance of the administration of small doses of iodine in the prophylaxis of goiter. Kraeuter in Munich has advised giving small doses of iodine to school children. Miesbach considers it the duty of the state to carry out this simple prophylaxis —J K

(THYROID) A case of retrosternal goiter (Ein Fall von retrosternalem Kropf) Molnár (A L), Klin Wchnschr (Berl), 1922, 1, 420

Description of a case —J K

Functional diagnosis of the THYROID (Funktionelle Diagnostik der Schilddrüse) Neuschloss, München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1281

In athyroidism the viscosity of the serum is largely increased. In Graves' disease the viscosity is slight —J K

Basal metabolism study of a case of congenital myxedema treated with THYROID extract (Étude du métabolisme basal dans un cas de myxoedème congénital traité par l'extrait thyroïdien) Nobé-

court & Janet (H), Bull et mém Soc méd d hôp de Par, 1922, 46, 608-611

A study of the basal metabolism of a 14 year old idiotic child weighing 26 kilos and 1 05 meters tall The tissues were infiltrated, the skin was dry, the face moon-like Thyroid opotherapy had produced no benefit Nevertheless the administration of thyroid extract (dose or preparation not given) did raise the basal metabolism from the low point of 37 8 to a high value of 52 8 —F S H

(THYROID) Goiter prophylaxis (Zur Kropfprophylaxe) Oswald (A), Schweiz med Wchnschr (Basel), 1922, 52, 313

Oswald summarizes the work of the American observers and states that his position regarding the use of iodine has been misinterpreted, in that he is not opposed to the use of iodine in goiter, but that it should be used with great caution and in very small doses He refers to Klinger's use of iodostarrin tablets, but prefers to use one to two milligrams of sodium iodide weekly in schools This is a very simple and exceedingly cheap procedure He reviews the possibility of other vehicles of administration of iodine as candies, salt, etc, and states that desiccated thyroid in exceedingly small doses is highly efficacious but too costly for general use (It might also be stated that it is too dangerous to be recommended for goiter prevention generally) He believes that the work thus far accomplished brings the prevention of goiter within the reach of possibility Whether the administration of iodine will succeed in entirely eliminating goiter is a question which will have to be decided by future generations It is certain, however, that endemic goiter will be greatly reduced and in this direction much has already been accomplished —D M

The oculo-cardiac reflex in HYPERTHYROIDISM and experimental hypothyroidism in the rabbit (Le réflexe oculo-cardiaque dans l'hypertyroïdie et l'hypothyroïde expérimentales chez le lapin). Parisot (J), Richard (G) & Simonin (P), Compt rend Soc de biol (Par), 1922, 86, 593-594

In the normal rabbit, compression of the eye causes a slowing of the pulse, varying with the subject, from 8 to 20 pulsations A single intravenous injection of 0 5 gm of thyroid extract causes an exaggeration of the reflex After a series of ten subcutaneous injections in twenty days, the reflex is very much less or slightly inverted After thyroidectomy there is an exaggeration of the reflex followed in ten seconds by a secondary acceleration of the pulse for thirty seconds or more The same is true for incomplete thyroidectomy In thyroidectomized animals, compression thirty seconds after the intravenous injection of 0 5 gm thyroid extract causes a slowing of the pulse, but less marked than the preceding, the secondary phase of acceleration is not marked Injection of adrenalin sup-

presses or inverts the oculo-cardiac reflex during the phase of excitation of the sympathetic, but the reflex reappears slightly after return of the blood pressure and pulse to normal —T C B

(THYROID) Incomplete form of myxedema, (*Über inkomplette Formen des Myxödems*) Perl (J E), *Ztschr f ges Neurol u Psych*, 1921, **71**, 268, *abst*, *Monats f Kinderh*, 1922, **22**, 758

Perl discusses several cases of what Hertoghe has called benign chronic hyperthyroidism. There are found in various combinations obesity, dermatitis, loss of hair, general trophic and menstrual disturbances. Thyroid therapy was followed by rapid amelioration —R G H

(THYROID) Basal metabolism and ideal weight and pulse ratio as shown by the findings in more than twenty-five hundred observations on about twelve hundred subjects. A preliminary report Peterson (Anne) & Walter (W), *J Am M Ass (Chicago)*, 1922, **78**, 341-343

Interesting tables and diagrams embodying the investigations suggested in the title lead the authors to the following conclusions. Basal metabolism determination by tried out portable apparatus is reliable as checked by the closed circuit, gas analysis method. The mass of evidence is against weight being influenced to any consistent degree by thyroid activity alone. The pulse rate and basal metabolism are closely associated generally —W M A

The Kottmann reaction for THYROID activity Petersen (W F), H'Doubler (F T), Levinson (S A) & Larbe (J E), *J Am M Ass (Chicago)*, 1922, **78**, 1022-1023

Kottmann's serum reaction was carried out on four hundred cases, made up of hyperthyroid cases, miscellaneous diseases and normal controls. Typical retardation of the reaction is given by over ninety per cent of the hyperthyroid cases and is very seldom found in other conditions. Border line cases were not available. The authors recommend the test as of clinical value —W M A

Influence of the spleen, kidneys, and THYROID on anaphylactic shock (*L'influenza della milza, del rene, della tiroide nella produzione della crisi anafilattica*) Pistocchi (G), *Pathologica (Genova)*, 1920, **12**, 239-240, *Arch per le sc med (Torino)*, 1921, **44**, 91-123

With beef serum as antigen, neither preceding splenectomy nor nephrectomy influenced definitely the anaphylactic picture in the guinea pig. Removal of the thyroid, however, diminishes the sensitivity of the animal to the anaphylatoxin —Chem Abst, **16**, 1459

(**THYROID**) Congenital goiter Report of four cases Porter (W B) & Vonderlehr (R A), *Am J. Dis Child* (Chicago), 1921, 22, 477-481

The authors report four cases of congenital goiter in boys, aged 3½, 6, 8 and 14 years, occurring in the southwestern part of Virginia, where goiter is endemic In the first case only did the mother of the child have a goiter None of the boys presented any symptoms of either hypo- or hyper-thyroidism, any mental aberration or abnormal development Especially noted was the lack of any toxic or pressure symptoms All the goiters were symmetrically enlarged, the most prominent part being the isthmus The consistency of the enlargement was soft but suggestive of the colloid type *Ascaris lumbricoides* was found in the stools of all of the children —M B G

HYPERTHYROIDISM in puberty (Das Pubertätsbasedowoid) Pototzky (C), *Deutsche med Wchnschr* (Berl), 1921, 47, 96-97

Between the harmless swelling of the thyroid in puberty and real Graves' disease the author describes the "Hyperthyroidismus pseudochloroticus" Here we find a soft, large thyroid, a pale color and complaints of fatigue, but without chlorotic changes in the blood Between this and Graves' disease the author describes

"Pubertätsbasedowoid" Both "hyperthyroidismus pseudochloroticus" and "Pubertätsbasedowoid" are seen much more in girls than in boys In the latter case there is a certain degree of exophthalmos, but no tachycardia Nervous complaints, abdominal pains, restlessness, insomnia and perspiring are very frequent Often these symptoms disappear with the onset of menstruation Treatment with iron or arsenic is not successful Good effect is seen from the ingestion of ovarian preparations —J K

(**THYROID**) A case of intratracheal struma (Ein Fall von Struma intratrachealis) Fuhr (L), *Klin Wchnschr* (Berl), 1922, 1, 875

A short note without details —J K

(**THYROID**) Hypothyroidism Rietschel, *München med Wchnschr*, 1922, 69, 180

A boy of 15, 109 cm in height, with a good intelligence, had symptoms of myxedema and retarded ossification of the metacarpal bones —J K

(**THYROID**) The physiology of hibernation (Ein Beitrag zur Physiologie des Winterschlafes) Schenk, *Klin Wchnschr* (Berl), 1922, 1, 659, *München med Wchnschr*, 1922, 69, 530

During hibernation animals have a low respiratory quotient The same is seen in rabbits after thyroidectomy Injections of thyroid, thymus or adrenals increases metabolism in such a way as to

awaken them Animals that hibernate have an endocrine system that easily becomes insufficient and causes them to become lethargic when exposed to very low or to very high temperatures —J K

Influence of the THYROID on creatin and creatinin metabolism (Der Einfluss der Schilddrüse auf den Kreatin-Kreatininumsatz) Schenk (P), München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1281

After ablation of the thyroid in rabbits less creatin and creatinin is excreted After administration of extract of thyroid the secretion of creatin and creatinin is increased —J K

(THYROID) A case of enormous goiter (Ein Fall von übergroßer Struma) Schloffer, Deutsche med Wchnschr (Berl), 1922, 48, 616, Wien klin Wchnschr, 1922, 35, 261

Demonstration of a case No details are given —J K

(THYROID) Technique of operation for goiter (Zur Technik der Kropfoperation) Schloffer (H), Beitr z klin Chir (Tübing), 1922, 125, 249-269

Of technical surgical interest —J K

(THYROID) Sporadic cretinism and hypothyreosis (Sporadischer Kretinismus bei Hypothyreose) Schmincke, München med Wchnschr, 1922, 69, 65

No details are given —J K

Functional study of the THYROID (Funktionsnachweis und Funktionsprüfung der Schilddrüse) Starlinger (T), Wien klin Wchnschr, 1922, 35, 473

Herzfeld and Klinger have propounded a theory that the first product of decomposition of protein of the different organs is fibrinogen In 15 cases Starlinger has compared the fibrinogen content of the blood in the arteries and veins of the thyroid In hyperthyroidism the fibrinogen in the veins is diminished, in hypothyroidism it seems to be increased Also the time necessary for the precipitation of the corpuscles ("Blutkörperchensenkungsgeschwindigkeit") is different in the arteries and the veins of the thyroid, and this difference seems also to depend upon the function of the thyroid Therefore, it is possible that the study of colloid chemical differences between the arterial and venous blood of the thyroid is of great importance in investigating the activity of this gland As 15 cases are too small a number for definite conclusions, the author intends to control and extend his series —J K

(THYROID-GONADS) True dwarfism (Über echten Zwergwuchs) Sternberg (C), Beitr z path Anat u z allg Path (Jena), 1920, 67, 275-308

Description of a number of cases of dwarfism The different effects of thyroidism and hypothyroidism, and the altered structure of the testes are considered —W J A

Sensitiveness of the **THYROID** to **ADRENIN** and exposure to γ -rays
(Beeinflussung der Adrenalinempfindlichkeit durch Bestrahlung der Thyreoiden) Szego, München med Wchnschr, 1922, 69, 723

The reaction after adrenalin depends upon the function of the thyroid When the thyroid of persons with sympathicotonia is exposed to γ -rays, no reaction is seen after the injection of adrenalin —J K

(**THYROID**) Cases of Graves' disease (Tilfælde af Mb Basedowii)
Trier (K), Hosp-Tid (Copenhagen), 1921, 64, 48

Between 1913 and 1920 Trier has treated about 200 cases of Graves' disease at the Rontgen department of the Rigshospital in Copenhagen In the course of two months he has personally examined 88 of these patients, and he has received reports on several others A comparison of the results showed that there was little to choose between giving (1) small exposures over a considerable period, (2) small exposures over a considerable period, the thymus being included, and (3) big exposures, both the thyroid and thymus areas being included Trier's opinion of the value of γ -ray treatment is guarded, it may be an excellent supplement to general medical treatment, giving this in many cases just the support needed to tip the scales in the patient's favor But it is not of epoch-making importance, and it seems to matter little whether the thymus is treated or not —Med Sci, 6, 175

Accessory **THYROID** growing in oesophageal lumen Whale (L),
Proc Roy Soc Med (Lond), 1922, 15, Sect Laryngol, 7

The aberrant thyroid was about the size of a cherry in a woman aged 58 It caused obstruction until removed —Physiol Abst, 7, 50

Water and salt metabolism during treatment with **THYROIDIN** and extract of **OVARY** (Beobachtungen des Wasser und Salzwechsels bei Thyreoidin und Ovarialextraktbehandlung) Veil (W H) & Bohn (H), Deutsches Arch f klin Med (Leipz), 1922, 130, 212-234

Thyroidin was administered and extremely exact examinations were carried out in two patients Both gradually lost weight, though one much more than the other There does not exist a parallelism between diuresis and loss of weight The patient who lost comparatively little flesh showed a real polyuria The quantity of nitrogen taken with the food was smaller than that excreted The loss of weight was due only to an increased protein metabolism In both cases the hemoglobin content of the blood remained un-

changed, though the amount of water of the blood was increased, as was proved by the determination of the amount of protein in the blood. The experiments show that the loss of weight during the first days is due to an increased loss of water and NaCl, later, however, only the increased decomposition of proteins causes loss of flesh. During these experiments the pulse rate is slightly increased, after some days of ingestion of thyroidin the blood pressure sinks. When *ovoglandol* is given hyperchloruria with polyuria and loss of weight is often seen. The serum then becomes poor in NaCl. These symptoms, however, are seen after some days and may be preceded by a gain in weight. The first day that *ovoglandol* is taken the excretion of NaCl is increased, either to a very slight or very marked degree, after which it is not always the same. When the ingestion of *ovoglandol* ceases, polyuria with a urine of normal concentration occurs. In this way much NaCl is excreted. The authors further point out how very small doses of thyroidin in myxedema or athyroidism may produce marvels, while much larger quantities of thyroidin have little or no effect in cases of so-called minor thyroid insufficiency. It is necessary to be very careful to make this diagnosis (introduced into pathology by Hertoghe). Even in complete athyroidism no adiposity is seen, therefore, the use of thyroidin in treatment of adiposity is explained by its influence on water and protein metabolism.—J. K.

(**THYROID**) Drainage nach Strumektomie Vidakovits (C),
Zentralbl. f. Chir. (Leipz.), 1922, 49, 157-161

Of technical interest only.—J. K.

(**THYROID**) Treatment and prophylaxis of endemic goiter (Behandlung und Prophylaxe des endemischen Kropfes) Wagner-Jauregg,
Wien klin. Wchnschr., 1922, 35, 369-370

In goiter belts the government should supply to the public kitchens salt containing about 2 mg. of KI or NaI per kilogram NaCl.—J. K.

The abstracts in this number have been prepared by the staff assisted by

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INVITATIONS TO RESEARCH IN ENDOCRINOLOGY

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Among the permanent satisfactions in the life of an investigator are the habit of looking forward towards the next steps in the progress of discovery, and an optimistic faith that the progress of discovery is of prime importance for securing control of natural events, especially when these events have a high degree of significance for the welfare of our fellow beings. Such are the central interests of those who are pioneering in the unexplored territory of internal secretions. There is no doubt of the value of more knowledge in this new territory. The endocrine organs play an essential rôle in fundamental processes—in the growth of the body, in the development of the nervous system, in the orderly succession of physiological states resulting in reproduction, in the mobilizing of the forces of the organism for physical struggle, and in the rate and character of the chemical changes occurring in the metabolic overturn. The endocrine organs are commonly referred to as the “controllers” or the “regulators” of these processes. As I have pointed out elsewhere, however, we must not be misled by these terms. In normal existence no organ has a supreme control. It is bound in a web of interrelations which permit it to be influenced in different ways and

which in turn permit it to influence other organs. Indeed, only through the filaments and channels which hold the separate parts together in a unity does each part have any significance. On the basis of these considerations we are justified in seeking methods by which we can control these potent "controllers," by which we can regulate the "regulators."

When there are so many "next steps" to be taken, when what we really know is so slight compared with what we should know, when the problems to be attacked are so evident, as is the case in the endocrine field, it may seem an elaboration of the obvious to consider the work to be done. There is always the possibility, however, that in the course of such a consideration some one may become interested and be stimulated to undertake research. That is the possibility that the investigator, eager to push forward in his labor, always feels justified in exploiting. Accordingly I propose to consider some opportunities for investigation in what seem to me the most important questions at present confronting us.

NERVOUS CONTROL OF INCRETION

A central problem is that of the nervous government of internal secretion. We now have evidence that the adrenal medulla, the liver and the thyroid gland can be stimulated to extra activity by sympathetic impulses. This knowledge at once gives us fresh insight, for such impulses are sent forth under pain, asphyxia and emotional excitement. And we find, in fact, that these conditions, associated with activity of the sympathetic system, are also associated with signs of activity in these glands. (1) Adrenin is discharged by the adrenal medulla, sugar and a pressor material are released from the liver, and some substance is given off by the thyroid which speeds up the rate of beat of the denervated heart.

There are other endocrine structures described as having a nerve supply to their cells. Berkley (1894) figured fine nerve filaments ending in knob-like enlargements on the surface of the cells of the anterior lobe of the hypophysis. (2) The cells of the parathyroids likewise are said to be well innervated. Both organs have a rich blood supply, such as that found in the adrenal medulla and in the thyroid glands, i. e., they are arranged for quick secretion. Doubtless these nerves have functional im-

portance, but we are entirely unacquainted with their action. The cells of the islands of Langerhans, according to Pensa (3), are surrounded by a basket-work of nerve fibers. These fibers presumably serve some purpose. Attempts to demonstrate any influence of sympathetic stimulation on the blood-sugar level, however, have thus far proved futile. De Corral's (4) observation that vagus stimulation induces a drop in blood sugar offers a valuable suggestion as to the nature of the innervation of the island cells. The work should be repeated, however, and carefully controlled, and if confirmed, the effect should be tested under more nearly physiological conditions by means of vagus reflexes.

A histological study relative to nervous control of internal secretion should include a careful systematic search for nerve filaments distributed to the cells of glands not yet known to be innervated. It is reported that the interstitial cells of the testis are not supplied with nerves (5). Possibly the cells of the adrenal cortex belong with them. If there is a group of endocrine structures of this type we might be able to classify the glands according to the presence or absence of nervous control. The former might exhibit both chemogenic and neurogenic secretion, the latter would be subject solely to chemical or humoral influences, i. e., would be pure chemo-endocrine organs. Definite progress would result, I believe, from such a classification, if it could be justified, for innervation of the endocrine glands probably means, as in the case of other glands, that they can be brought into special service in time of need. Possibly endocrine activities strictly chemogenic in origin are manifested in rhythmically repeated processes as, for example, in the functioning of the ovaries, where a special or extra display would be of no advantage.

DRUG CONTROL OF INCRETION

In relation to nervous and humoral control of the ductless glands is their control by drugs. Here we are only at the beginning of what may prove to be a big advance. About ten years ago, in collaboration with Aub and Binger, I published a brief note presenting evidence that small doses of nicotine would cause secretion from the adrenal medulla (6). This testimony was soon confirmed by Dale (7), and later by Stewart and Rogoff (8).

These last observers have reported that strychnine (9) and physostigmine (10) also call forth an extra discharge of adrenin. Since the effects of these drugs are produced through their influence in rousing sympathetic impulses, the probability is strong that they can be shown to affect also the liver, and the thyroid gland. Mills has reported, indeed, that there are histological changes in the thyroid after exhibition of strychnine, and has stated that morphine and quinine appear to decrease the activity of the gland (11). The effects of these drugs, however, should be tested by physiological methods. An interesting enquiry lies here.

The influence of anesthetics should be further studied. Ten years ago Elliott reported that ether, chloroform and urethane would cause exhaustion of the adrenal medulla, an effect mediated by the splanchnic nerves (12). A number of improvements in methods of determining adrenal secretion have been made in the last decade, and because Elliott's method has been questioned (13), it is desirable that the influence of anesthetics be again studied, not only in relation to adrenal, but also in relation to hepatic and thyroid activity.

Before leaving the subject of the control of endocrine organs by drugs I wish to allude to one very important achievement, which can be placed to the credit of American investigators—the prevention of simple goiter by means of sodium iodide, as recommended by Marine and Kimball (13). This is an admirable illustration of what may be accomplished when carefully established knowledge has bestowed its reward by giving us power to lessen the ills of both man and lower animals.

INFLUENCE OF DIET ON INCRETIONS

Another line of work which seems promising is that concerned with the influence of diet. Although there is physiological opinion that the liberation of glucose from the liver is not a true internal secretion, because no peculiar new substance is evolved by the hepatic cells, nevertheless the process is related historically in a significant degree to the beginnings of our ideas of internal secretion. It was with reference to this process that Claude Bernard, in 1859, first employed the expression "*sécrétion interne*". The sugar which can be set free from the liver is stored there in the form of glycogen when the carbohydrate sup-

ply is sufficiently abundant to permit. There appears to be a similar storage of protein, according to the observations of Berg (15) and of Stubel (16). They noted that feeding protein food or even amino acids leads to an accumulation of protein material in the liver. Stubel's discovery that this material is discharged by subcutaneous injection of adrenalin further emphasizes the possible relations of diet to internal secretion. Of course, in diabetes we have had for many years evidence that a mild case can be converted into a severe one by feeding carbohydrate food in amounts surpassing the ability of the organism to metabolize it. This appears to be due to an overpowering demand on the islet cells of the pancreas (17). But what this "demand" really is, how the islet cells are brought into action by the taking of food, needs to be determined. Fortunately, the recent highly important work of Banting, Best and Macleod (18), which has resulted in the isolation of a hormone from the pancreas that is capable of promptly reducing the hyperglycemia of diabetes, promises much light and may lead to new information regarding the insular response to carbohydrate feeding.

The influence of diet on other secretory glands is still largely unknown. Watson has reported that the thyroid of the wild rat may be made to lose practically all its colloid by feeding bread and milk (19). Burget confirmed this observation, but had to keep the animals in an unhygienic condition in order to obtain the result. He found, however, that thyroid hyperplasia could be readily produced by a high protein diet (20). Tanberg likewise has noted marked hypertrophy of the thyroid in cats fed for several months exclusively on meat (21). By giving pregnant sows mainly protein food Hart and Steenbock (22) have produced pigs without hair—a condition which, along with thyroid and other disorders, is observed in our western plains where the iodine supply in the food of domestic animals is deficient. In other words, protein feeding appears to make a demand on the thyroid that is equivalent to depriving the gland of necessary iodine. Possibly these observations can be put to use in controlling thyroid disorders. Rosenbloom (23), indeed, has suggested that in the treatment of "hyperthyroidism" a diet with a low iodine and minimum protein content be given. Clinical studies on this point might yield valuable results.

Physiologists have long known that starvation causes a loss

of weight in most of the organs of the body, with the heart and the central nervous system as notable exceptions. Recent researches have revealed that the adrenal glands, the thyroid and perhaps the pituitary body actually become larger during inanition. McCarrison (24) first reported hypertrophy of the adrenals in pigeons deprived of food, an observation soon confirmed by Vincent and Hollenberg. They state that starvation for 15 days doubles the weight of the adrenals of pigeons, and that it produces similar hypertrophy in rats and dogs (25). Soldiers who died in prison camps, where they had been poorly fed, likewise showed this effect, with the enlargement chiefly in the cortex (26). According to Vincent and Hollenberg the adrenin content of the adrenals was at first increased by inanition, but later was greatly reduced. The thyroid glands, though hypertrophied, were almost lacking in colloid (27). Sheep, inadequately fed, have been reported as having thyroids with a much smaller amount of iodine than normal (28). And in advanced inanition there may be marked hydropic degeneration of the gland cells (29).

The effects of deprivation of food may be largely due to absence of certain vitamins. McCarrison's studies on pigeons, guinea pigs, and monkeys have shown that a diet deficient in vitamins will induce enlargement of the adrenal glands and, in the male, of the pituitary as well (30). There is not time to consider these interesting studies in detail. These examples suggest promising opportunities for further valuable work on dietary control of the endocrine organs.

In relation to adrenal enlargement from starvation, the enlargement from feeding thyroid substance may be mentioned (31). In both conditions a mechanism to protect the bodily reserves would be advantageous—some device for reducing the rate of chemical destruction when the food supply is lacking and also when the burning of the supply is being overstimulated. It may be that hypertrophy of the adrenal cortex is related to such a protective service. The suggestion of Shapiro and Marine (32) that in exophthalmic goiter there is a relative functional insufficiency of the suprarenal cortex may have pertinence in this relation. Before we are justified in drawing any definite conclusions, however, these hints must be worked out and the degree of their correspondence to actual fact established.

The origin of the active agents of the internal secretions is a matter of considerable interest. Before much work can be done on this topic, however, we shall have to know more about the chemical composition of the various gland products. In the case of adrenin it happens that we have learned that the chemical structure closely resembles tyrosine. Possibly feeding experiments, in which this one of the amino acids is given in excess or is withheld for some time, would induce corresponding changes in adrenin formation.

SEASONAL VARIATION OF INCRETORY FUNCTIONS

A highly interesting aspect of endocrine function which needs to be systematically examined is the seasonal variation of activity. The most striking illustration of this phenomenon is that afforded by the changes which accompany breeding. The approach of the breeding season in many animals is manifested by a greatly increased activity. Male birds perform strange antics or rapid flights, probably from the operation of some internal impulse (33). Secondary sexual characteristics are developed at this time. "In the spring a livelier iris changes on the burnished dove"—a change doubtless associated with the functioning of the interstitial tissue of the gonads. The stags have fully developed antlers at the time of rut; during that season they are in a state of constant excitement, fighting one another for possession of the hinds. A month or two later, when the excitement and fighting have ceased, the stags once more herd together peaceably, and shortly thereafter the antlers are shed. Since antlers are prematurely shed as a consequence of castration, and thereafter fail to grow, this culminating process, occurring in the red deer in September and October, may properly be regarded as evidence of seasonal recurrence of endocrine activity. Catlin's description of the analogous period, as it used to occur in herds of bison many years ago, is so vivid that I cannot forbear quoting it:

"The *running season*, which is in August and September, is the time when they congregate in such masses in some places as literally to blacken the prairies for miles together. It is no uncommon thing at this season, at these gatherings, to see several thousand in a mass, eddying and wheeling about under a cloud of dust, which is raised by the bulls as they are pawing in the dirt or engaged in desperate combats, as they constantly are, plunging and butting at each other in

the most furious manner. In these scenes the males are continually following the females, and the whole mass are in a constant motion; and all bellowing (or 'roaring') in deep and hollow sounds which, mingled together, seem, at the distance of a mile or two, like the noise of distant thunder" (34)

Again we must regard this extraordinary behavior as being determined by a seasonal appearance of endocrine function

There is evidence that in the lower primates and also in uncivilized man a breeding season exists. Among primitive peoples annual festivals—usually in the spring—were attended by great sexual license, and may have been the outcome of the awakening of powerful impulses at that time. Even in civilized conditions there are some indications of a pairing season. The largest number of births usually falls in the month of February, corresponding to conceptions in May and June. Statistics from Sweden indicate the largest number of conceptions in June, whereas statistics from Greece and Italy point to April and May as the time when they occur most frequently, i. e., the farther south the earlier the period (35). It is remarkable that in spite of the great gaps which separate modern man from the influence of climatic changes—because of clothing and shelter, warm houses and continuous food supply—there should still persist indications of a seasonal periodicity of the reproductive function. Possibly the effects of seasons are to be seen in a more striking degree in cold climates than in warm or tropical regions, and perhaps among rural populations, more exposed to climatic changes than are the city dwellers. Statistical studies of these possibilities might yield very suggestive results.

We have also highly interesting evidence of seasonal variations in the thyroid gland. In 1913, Seidell and Fenger reported that in general there is from two to three times as much iodine in the thyroid glands of cattle, hogs and sheep during the months between June and November as during the months between December and May. The months showing a maximal content were September and October, those with a minimal content were March and April (36). Fenger has more recently confirmed these observations and has shown that the average maximal iodine content is about ten times the minimal quantity for cattle, about seven times for sheep and two and a half times for hogs (37). In this connection a recent experience of my own may be cited. Smith and I had found that massage of the cat's

thyroid gland or stimulation of it by conditions arousing nerve impulses in the cervical sympathetic strand would accelerate the denervated heart. The observations were made chiefly in December. Attempts to repeat the experiments with massage in March and April gave slight or negative results. We are now looking forward to the autumn months with great interest.

Fenger is inclined to attribute the variations chiefly to the effects of temperature, for in cattle and sheep, though not in hogs, the onset of cold weather is followed within a week or two by a noticeable enlargement of the thyroids and a lowering of the iodine percentage. The observation of Mills (38) that rabbits, guinea pigs and cats, though kept on a constant diet, showed signs of increased thyroid activity when subjected to cold, the testimony of Loeb that compensatory hypertrophy of the thyroid of guinea pigs after extirpation of most of the gland is less in the warmer months (May to October) than during the winter (39), and the changes noted by Hart—a decrease of the size of the thyroid and a disappearance of the colloid in mice when kept in a warm atmosphere, with signs of greater activity in cold surroundings (40)—all these experimental results lend support to the conclusion that seasonal variations of temperature may effect to a marked degree the activities of the thyroid gland. On the other hand, Reid Hunt noted striking seasonal changes of thyroid function, in *opposite* directions for guinea pigs and mice, as revealed by his acetonitrile test, when the animals were fed on a fairly uniform diet and kept in the laboratory under fairly constant temperature conditions (41). He is inclined to attribute the annual thyroid rhythm, therefore, to other factors than diet or the annual temperature oscillations.

From the evidence in hand it is clear that there is work of great importance to be done in further examination of the seasonal changes in the gonads and the thyroid, as well as extension of the studies to other glands of internal secretion. We need to know how these changes may affect human cases. It is well known that pregnancy may bring on tetanic spasms in animals with deficient parathyroid tissue. McCarrison has reported that the endemic tetany of child-bearing women in the Chitral and Gilgit valleys of Northern India is practically confined to the spring months (42). Possibly the parathyroids undergo periodic alterations of functional capacity. A workman's tetany

has been described as occurring in parts of Germany and Austria in certain types of industry, it appears usually twice a year, in the spring and in the autumn. Although attempts have been made to explain the malady in terms of chronic ergotism, it is still mysterious. Possibly here also we are concerned with periodic endocrine changes.

If the thyroid and the gonads exhibit waves of seasonal activity, we should expect to find that the bodily processes influenced by them, such as growth and metabolism, would also manifest seasonal waves. Unfortunately the data which would give us insight into these relationships are still quite meager. The recent studies by Porter, on the growth of school children, may be significant of ups and downs in endocrine action. He has found that when the children are weighed month after month the gain in weight between September and January in both boys and girls is approximately four times the gain from February to June. Indeed, practically all the growth occurs in the autumn, and there appears to be almost a standstill during the late winter and early spring months.

So far as metabolism studies are concerned we have very little on which to rest judgments. To provide adequate data, the basal metabolic rate should be determined on the same individuals at regular periods throughout the year. Tests made upon W. W. P. in mid-winter and in mid-summer brought out the fact that his metabolism was considerably faster in the cold season (43). During an Arctic expedition Lindhard determined on himself the carbon dioxide output in half-hour periods under standard conditions. A series of ten experiments which show remarkable consistency was repeated every two or three months. He found that from April to September the standard metabolism was *increased* as compared with the winter months (44). These scattered observations on seasonal differences in growth and metabolism in man, though not concordant, may be very pertinent to our interest in endocrine effects. And they raise many questions. Are there winter conditions of the human thyroid that are different from summer conditions? If this is not the case in persons living protected lives indoors, or residing in warm parts of the country, may it be true of persons exposed to the severity of our northern winters—e. g., teamsters, brakemen and others whose labor changes little during the year. Pos-

sibly necropsy studies, preferably on subjects confined under controllable conditions, as in asylums and penitentiaries, would yield in time significant data. Again there are questions relative to the incidence and exacerbations of disease. For example, what evidence is there as to the influence of warmth and cold on the occurrence of thyroid disease? Would metabolism determinations reveal any effects of temperature and climate on the disturbed processes? These and other questions at once arise from the facts already ascertained.

RELATION OF AGE TO INCRETORY ACTIVITY

Another group of questions center around the relation of endocrine organs to the age period. We know that the metabolic rate is much more rapid in the child than in the adult, and that as middle life slips on towards senility the rate gradually falls. Are these changes associated with corresponding changes in the internal secretions? In old age does the thyroid, which pre-eminently influences the speed of chemical processes in the body, show signs of lessened activity? Starr regards the dryness of the skin, the brittleness of the nails, and the loss of hair, characteristic of the later years of life, as due to thyroid deficiency, and claims that they may be stopped by taking small amounts of thyroid substance (45).

When we come to the remarkable sequence of events which leads to maturity—the prepubertal increase in height, the development of secondary sexual characteristics, the increase of bodily vigor, the appearance of reproductive elements—remarkable transformations related to changes in the interstitial tissue of the testis, in the thyroid, in the adrenal cortex and in the pituitary body, as well as gradual disappearance of the thymus, we are confronted with a complex of interrelations altogether too involved to be untangled at present. We must rest on the faith that this wonderfully ordered process, starting on schedule time in the life history, after thirteen or fourteen years of quiescence, is automatically arranged to run its course. Some time we shall know, I believe, the successive stages, and be able to help them onward when they are checked.

HEREDITY AND THE INCRETIONS

Related to the influence of both age and season, as conditions affecting endocrine activity, is the inheritance of endocrine

defects According to Ennis Smith, what he called "fetal athyrosis"—the disorder of domestic animals already mentioned as characterized by lack of hair, by thin brittle hoofs, by low iodine content of the thyroid in the young—occurs in regions where goiter is more or less endemic It will be recalled that the iodine content of the thyroid in domestic animals is lowest in March and April and highest in September and October It is very significant that the litters of pigs born in March and April are more frequently affected with the disease than those born in May and June, and that even in quite unfavorable regions the litters born in the fall are usually normal The symptoms above described are suggestive of a congenital myxedematous state, occurring in the offspring of animals which have had an insufficient iodine supply in the food (46)

Already there is a considerable accumulation of clinical evidence of a similar linkage between a mother suffering from a defective thyroid and her child McCarrison has concluded from his extensive studies in Northern India that thyroid dysfunction in the mother is the essential factor in the production of cretinism These are observations which should be extended, not only in relation to cretins, but also in relation to other victims of endocrine disorders There is suggestive evidence that mongolism occurs in the later years of the mother's reproductive period, and that it, like cretinism, may be due to thyroid deficiency But again we are in need of more data, carefully gathered and evaluated

CRITERIA OF ENDOCRINE FUNCTIONS

Perhaps our most urgent need at present is the development of satisfactory tests of endocrine disturbance To a degree altogether too great we are compelled to judge mild cases by general impressions At least current literature indicates that diagnoses are made on relatively slight objective signs If Shelley had "a hyperthyroid face," as has been suggested, it would be well if we could all know just what a hyperthyroid face is Many years ago Galton suggested the possibility of registering general impressions by means of composite photography (47) It might be an enterprise of much interest to learn whether typical endocrine features could be registered by this means If

we must depend on appearances, this would seem to be a feasible method of learning the recognizable traits

We may not have to depend on such uncertain methods, however, for the internal secretions, as chemical agents, may in time be given adequate chemical tests. Meanwhile, we have already the beginnings of fairly satisfactory physical and biological tests. In skillful hands the basal metabolic rate is an excellent measure of thyroid variation from the normal. The test suggested by Goetsch (48), designed to reveal hyperthyroid activity, is criticized because it is positive in cases which do not have other indications of extra thyroid function (49). There is no question of the phenomena observed by Goetsch, but theoretically they may be due not only to hyperthyroidism but also to excessive activity of the sympathetic system and to increased secretion of adrenin into the blood. By properly conducted experiments, based on present control of these three factors, it might be possible to distinguish between them, and thus to refine the procedure. It is conceivable, indeed, that the Goetsch test could be made to apply to two conditions instead of one, and at the same time be more accurate than at present.

ENDOCRINE INTERRELATIONSHIPS

If the finding of objective tests of endocrine disorders is our most urgent task, the untangling of the net of endocrine relations is doubtless our most difficult one. The possibilities of mutual influence are so extensive, the clinical and experimental methods now available are so limited, the difficulties of closely reproducing in lower animals the disturbances seen in man are often so great, that we might well despair of ever solving the riddle. It seems to me, however, that we have certain general principles to go on. First, in the normal organism the orderliness is due to automatically adjusted equilibria. Second, in attempting to learn the operations of the factors concerned in an equilibrium we must consider each one not only by itself, but also in relation to all the others that are engaged in the same service. For example, growth is influenced by the interstitial tissue of the testis, by the anterior lobe of the pituitary and by the thyroid. We should expect, on the basis of what I have suggested, that these three organs normally work in co-operation, and that a disturbance in one would influence both

the process of growth and the relations of the other organs to that process. Possibly by classifying the endocrine glands on the basis of their common effects, their interrelations would prove to be simpler and less mystifying than they now appear and we should have sufficient insight to see where the threads which we have in our hands really lead us.

CONCLUSION

At the outset I spoke of two of the satisfactions in the life of the investigator—the forward look and faith that new knowledge gives new power. I might have added another satisfaction which he enjoys—the use of his imagination. Usually one engaged in research hesitates to mention the ideas he has projected because they so often prove to be futile. And if I may judge from my own experience, a number of the suggestions for new work which I have made above will prove to be futile. They were not made, however, because they represent certainty of results, but because they disclose attractive possibilities of investigation. If perchance anyone is stimulated to set about some task in relation to the problems we have been considering, my purpose would be secured. And if results should come from the effort, there would be especial satisfaction.

It is evident, I think, that there is no more interesting field for research in medicine or biology at present than that of internal secretion. It is a field which calls for both the laboratory worker and the clinician. One needs only to mention Addison and Graves, von Mehring, Koehler and Marie to prove that most of the early advances in endocrinology were due to clinical studies. The clinic presents types of disorder which the laboratory does not know. But the laboratory frequently offers the advantage of much simplified and more controllable conditions. In the studies which I have suggested, however, there are opportunities not only for clinicians and experimenters, but for histologists, and for statistical experts, for observers skilled in photography, and for biochemists. There is plenty for all of us to do. In a co-operative spirit we must push onward, continuing to apply the well-tried methods of critical observation, limited inference, and discriminating test, with the assurance that only thus shall we firmly establish the truth.

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THE GLANDULAR STATUS OF BROWN MULTILOCULAR ADIPOSE TISSUE

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This review seems justified by the fact that the brownish-colored and gland-like multilocular adipose tissue found in many mammals has repeatedly been considered to be an incretory gland and by the further fact that recently it has been suggested that it may be of importance in connection with deficiency diseases

NAMES BY WHICH IT HAS BEEN KNOWN

While this multilocular adipose tissue is most often termed the *hibernating gland* (Barkow), it is met with in the literature under a variety of other names—*adipose gland* (Rudolphi), *oil gland* (Jones), *brown fat* (Hammar), *lipoid* or *cholesterin gland* (Cramer), *organ of hibernation* (von Hansemann), and *hibernating mass* (Vignes). A circumscribed fat mass in human fetuses in the dorso-cervical and interseapular regions, which some consider a homologous structure, has been called the *inter-seapular gland* by Hatai. As will be evident from the following discussion, there is very little and frequently no justification for many of these terms. The safest designation at the present time would seem to be *multilocular adipose tissue*.

GENERAL STRUCTURE AND COMPOSITION

In gross appearance it resembles very much a lobulated gland such as a salivary gland. Its fatty character is not suspected till examined microscopically. It consists of densely packed cells, 25 to 30 micra in diameter, whose cytoplasm is greatly distended with fat globules. These cells are bound together to a large extent by an unusually close plexus of capillaries. It differs from ordinary adipose tissue in that the essential cells are multilocular, much richer in granular cytoplasm and smaller in size. The nucleus remains spherical and, while frequently very eccentric in position, is never flattened

against the margin Carlier and Evans (1903) could obtain only 40 per cent of fat by weight from this tissue in the case of the hedgehog as compared with a yield of 90 per cent often obtainable from ordinary adipose tissue. As might be expected, they found as high as 15 to 16 per cent protein in the hibernating gland. Shattock (1909) reports that the iodine value of the fat differs in the two types of adipose tissue. According to Vignes (1913) the fatty material in the hibernating gland of the rat is composed largely of a substance closely related to lecithin, probably jecorin. Cramer (1920) also stresses the presence of considerable cholesterol and other lipoids, and yet Carlier and Evans (1903) found in the hedgehog that nine-tenths of the fat in the hibernating gland was olein, the remainder being sterin with a trace of palmitin, lecithin and pigment. The greater amount of pigment in the multilocular fat may play some rôle in preserving the unsaturation equilibrium of the fats, as suggested by Currie (1922). Although Carlier and Evans also made determinations on the mineral content and the solubility of the fat, the chemistry of this tissue is too meager to warrant any general conclusions.

In hibernating animals the amount of fat present and hence the size of the cells and the whole structure vary with the season of the year. It is maximum just before the onset of dormancy. It decreases slowly during winter-sleep and then more rapidly in the spring as the animal becomes active. The whole tissue is thus reduced to about one-fourth of its former bulk. It also becomes much darker in color. The cells decrease from 30 micra in diameter to 10 micra. In this reduced condition the cells resemble epithelial cells with an abundant granular cytoplasm in which is an occasional fat globule. There is no evidence that any cells revert to fixed connective tissue cells. The nucleus remains spherical in shape and unchanged in size. As summer advances the cells become filled with fat again, the tissue becomes lighter in color, and returns to its former size.

While nerves have been described in the organ, especially by Carlier (1893), no nerve supply to the essential cells has been positively demonstrated. (For further details the reader is referred to a forthcoming publication on the hibernating gland to appear in the *Journal of Morphology*, Philadelphia.)

LOCATION AND DISTRIBUTION

Usually there is a large mass of this tissue in the superior mediastinum, about the thymus. Numerous small masses extend upward along the large vessels of the neck and in the intermuscular septa of the cervical region. By means of slender prolongations dorsal to the clavicle, the cervical portion is frequently continuous with a prominent lobe in each axillary fossa. These latter lobes may represent one-half of the entire organ. A pair of lobes is often found between the scapulae and extending forward between the dorsal muscles of the neck. From the mediastinal mass there are slender caudal extensions along each sympathetic chain, aorta, and mammary arteries. In some animals it may extend into the abdominal cavity and form two prominent perirenal lobes. Less frequently isolated masses are found lower down along the aorta and its main branches as far as the inguinal region.

Examination of the literature reveals the fact that it has been found in about 47 species (5 insectivora, 9 chiroptera, 33 rodentia), with some uncertainty in several more species. Since most of them are hibernating animals, the association of this structure with winter-sleep has been repeatedly made, but there is a large number of species (rats, mice, rabbits, etc.) that possess this structure and yet do not hibernate. On the other hand, the organ is not found in some mammals that do hibernate (e. g., European badger).

The locations most often mentioned are the thoracic and cervical. Next in order come the axillary and interscapular. It is still less often indicated in the renal, while the inguinal is least often the site.

ITS HOMOLOGY IN MAN

Rather distinct circumscribed fat masses in the posterior triangle of the neck and axillary and interscapular regions have been described in some detail by Merkel (1899), Charpy (1901), Hatai (1902), Bonnot (1908) and Shattock (1909). Hatai, Bonnot and Shattock consider these to be probably homologous to the hibernating gland of lower forms. Shattock believes that the fatty swellings in the neck and axilla of cretins are the same structures as the hibernating gland which he found in these locations in the hedgehog. These fatty masses in thyroid dis-

orders had been noted previous to this by T B Curling (1850) and again by H Fagge (1871) Cramer (1920) stresses the glandular character of the perineal fat, which, in the human embryo, appears to him to be essentially like the hibernating gland But the literature does not present convincing proof of the similarity in structure between these fat masses and the typical hibernating gland There is also some negative evidence Berg (1910), who made an extensive examination of human material, Batty Shaw (1902) and Auerbach (1902) were unable to see anything in man that resembled the brown fat of animals

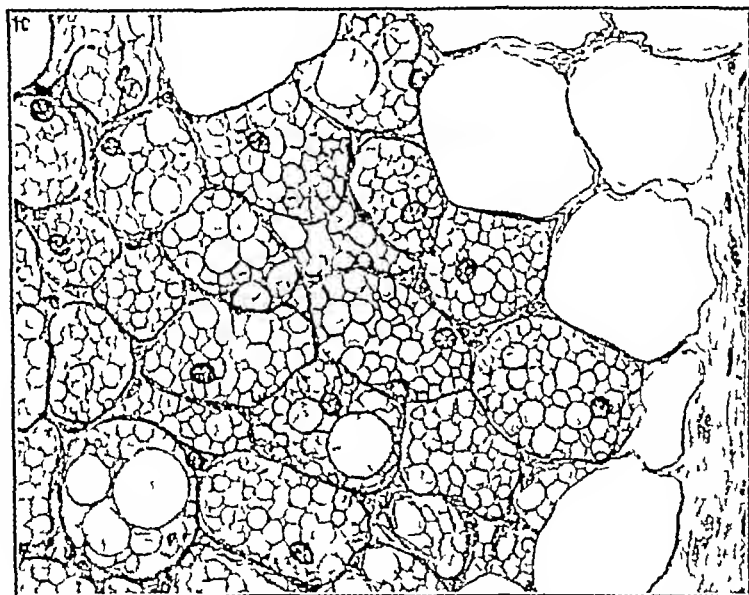


Fig 1 Camera lucida drawing of multilocular fat cells and a few ordinary adipose tissue cells from the perineal fat of a normal newborn child. Formalin fixation, celloidin, hematoxylin and eosin X 400 By comparing this figure with Fig 2 the similarity in structure between these multilocular fat cells and the essential cells of the so called hibernating gland of animals is clearly evident.

In spite of the above negations, there are occasionally in the perineal fat of newborn and very young children cells, as shown in Figure 1, which are in all structural details essentially the same as the typical hibernating gland cells (Fig 2) Just how often and how widespread such multilocular fat cells may be found in man no one can say for lack of sufficiently extensive examination of human material The cells here shown in Figure 1 are not developmental stages of ordinary fat, for in the latter case the nucleus is early crowded and flattened against

the cell margin and the dioplets coalesce into a larger and larger globule which fills most of the cell long before it reaches the size of those illustrated here. The relatively large amount of cytoplasm is also atypical of ordinary developing adipose tissue. Then, too, no intermediate stages are clearly seen.

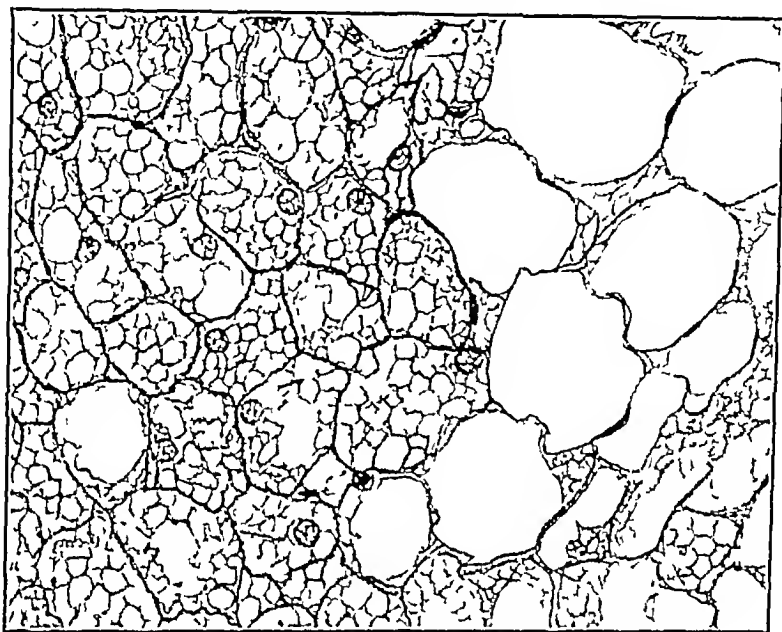


Fig 2 Camera lucida drawing of the brown fat or hibernating gland cells and a few ordinary adipose tissue cells from the common white rat. The relative abundance and multilocular character of the cytoplasm as well as the spherical shape of the nucleus in hibernating gland cells are well contrasted with the general appearance of the adjacent cells of ordinary adipose tissue. Except for greater shrinkage (due to paraffin embedding) this figure is strikingly similar to Fig 1, which is from a human subject.

DEVELOPMENT

Carher (1893) describes these hibernating gland cells in the hedgehog as coming from small round granular connective tissue cells, similar to those that give origin to ordinary fat cells. Hammar (1895) found the anlage of the interscapular lobe in the rat first to differentiate from the mesenchyme in embryos 1.2 cm in length, but fat droplets did not appear till the latter part of intrauterine life, when it accumulated rapidly. He was unable by feeding rats for three months on a diet rich in fat to change these cells into ordinary adipose cells. There always remained the wide cytoplasmic border. Von Hanseemann, who also utilized the rat, found the first trace of these multilocular fat cells in foetuses 1.6 cm in length in both the dorsal region of the neck

and the axilla. Later it appeared in the neighborhood of the thymus. The cells first appear as large polygonal cells of connective tissue origin. Large blood vessels are associated with these cells before they have differentiated. Both the place of development and the histogenesis, he claims, distinguish this brown glandular fat from ordinary adipose tissue. Bonnot (1908) described the "interscapular gland" in human subjects as arising from the walls of the primitive jugular vein. The tissue which forms in this region differentiates into lymphoid tissue and fatty lobules. The lymphoid tissue in turn develops into lymph nodes and hemolymph nodes. There seems to be no justification, however, for considering the lymph nodes as part of this fatty structure.

FUNCTIONAL SIGNIFICANCE

This gland-like adipose tissue was first mentioned by Velsch in 1670. He thought it was of a lymphatic nature and functionally related to the thymus. The next three writers on the subject (Harder, 1686, Scheuczer, 1727, Buffon, 1749) make no comment on its function. Sulzer (1774) spoke of it as a gland, Pallas (1778), Meckel (1806, 1815), Mangli (1807), Prunelle (1811), and Tiedemann (1815) considered it a part of the thymus.

It was Ludwig Jacobson who, in 1817, first clearly showed that it is a distinct structure and not a part of the thymus. He demonstrated that in marmots, hedgehogs and bats the thymus undergoes the usual involution and in its place develops a fatty tissue which varies in size with the season of the year. This work was repeated by Haugstedt (1831), who fully corroborated the findings of Jacobson. Rudolphi (1830) and Wagner (1835) similarly considered it as only a modified form of adipose tissue, but Burdach (1830), Simon (1845) and Jones (1852) adhered to the old notion that it was a persistent thymus, although Simon recognized that it may become changed to a mass of fat cells.

Barkow (1846) was the first to call it the hibernating gland. Although he recognized that it was a separate organ from the thymus, he considered that it belonged with the ductless glands such as the thymus, thyroid, etc. That it is a separate structure from the thymus, but still a ductless gland probably of the haemopoietic series, was also the belief of Ecker (1853), Valen-

tine (1857, 1859), Leydig (1857), Friedleben (1858), Vogt and Yung (1894) and Wiedersheim (as late as 1907)

Stannius (1853) had the peculiar notion that the sympathetic nervous system developed from its interior

Beginning with Hirscl and Frey in 1863, the hibernating gland has in general been regarded as a variety of adipose tissue probably serving merely as a source of food during winter-sleep. From histological studies, Hirscl and Frey decided that there is no similarity between this fatty tissue and lymph- or blood-forming organs in general and the thymus in particular, although their idea of the finer structure was entirely erroneous. Sharing very much this same idea of its functional significance are Owen (1868), Fleischel (1869), Afanassiew (1877), Ehrmann (1883), Poljakoff (1888), Carlier (1893), Hamman (1895), Dubois (1896), von Hansemann (1902), Auerbach (1902) and Polimanti (1912). Polimanti suggests that it may also act as a protective cushion enveloping the thorax and thus guarding the internal organs from the external temperature.

Its importance as a special source of food for the hibernating period has, however, been greatly overestimated, at least as far as the amount of material that it yields is concerned, as is evident especially from the figures given by Valentine (1857, 1859). This investigator found that the hibernating gland of the European marmot, while giving up nearly 70 per cent of its weight as food during winter-sleep, represents, to begin with, only 1.33 per cent of the total body weight. Calculations from his figures show that ordinary adipose tissue contributed 20 times as much material during the same time and skeletal muscle 8 times as much and the liver 2 times as much as the hibernating gland. Since other tissues also yield food material it follows that less than one-thirtieth of the consumed body tissues came from the hibernating gland. Carlier (1893) gives somewhat higher figures for the hedgehog, in which the structure represents about 3 per cent of the body weight before hibernation and decreases during dormancy to about 1 per cent.

A number of other investigators (Aeby, 1875, Harvath, 1878, and Ballowitz, 1891) of this period do not commit themselves on the physiological phase of the question.

Although the notion that the hibernating gland is a persistent thymus and the later idea that it is a separate organ but

still of the haemopoietic series were discarded, the theory that it is a gland of some sort persisted. Thus Malesani (1902) was struck with its glandular appearance and considered it to be a ductless gland which was of great importance during hibernation. Shattock (1909), because of the discrete droplets of lipid which its cells contain, thinks it is allied to the ductless gland, and since it does not behave like ordinary adipose tissue (being spared during the major portion of the dormant period) it is physiologically as well as histologically specialized. Salmon (1910, 1916) argues that it is the only organ that is active during winter-sleep and functions as a true endocrine organ by inhibiting all other glands of internal secretion.

Vignes (1913), from the experiments reviewed in the next section of this paper, concluded that the organ may be considered an economizer of proteins by insuring the utilization of reserved carbohydrates and fats first. This suggestion is interesting in connection with more recent work on the rôle of ordinary fats in the utilization of proteins by diminishing their toxicity and increasing their availability, as argued by Maignon (1921).

Finally Cramer (1920) lays stress upon the fact that the fatty material is rich in cholesterol compounds and other lipoids and that this lipid is retained during ordinary starvation, but is used up in animals dying for lack of accessory food factors. He suggests that the lipid has been used up to supply vitamins. From the great similarity in the reaction to polarized light between the suprarenal cortex and this multilocular fat, he assumes that there is also great similarity in composition.

EXTIRPATION EXPERIMENTS

Apparently the first extirpation experiments on record in connection with this multilocular fat tissue are those by Dubois (1896), who first merely exposed the structure in the marmot to see the effects of the necessary preliminary operative procedure. On the following day as much of the tissue as possible was removed. Two of the animals lived two or three days and during this time they exhibited no difficulty in warming up rapidly after torpor.

Auerbach (1902) extirpated the dorsal part of the hibernating gland in a rat. The animal lived two months. There was no regeneration of the lost tissue, its place being occupied by ordinary adipose tissue.

As the results of an extensive series of extirpation experiments in connection with the utilization of extracts of the hibernating gland on white rats and mice, Vignes (1913) found that while most of the rats survived the removal of a large part of the organ (it is improbable that complete removal could be achieved) they lost weight and finally died. Only two lived more than three months. One lived four and one-half months. In the mouse, in which the operation is more difficult, the animals survived indefinitely, although there was an initial loss of weight. The rats operated upon had an increased resistance to adrenalin and cobra venom and a lessened resistance to chloroform. He also found that the extract of this fatty tissue increased the toxic power of tetanus toxin. The organ also apparently modified enzyme action for its extirpation diminished the quantity of lipase in the serum of the rats. It contained a lipase which acted on monobutyrin. The amylolytic power of the serum of the experimental rats was diminished, but extracts of the organ did not act on starch. The extract had an antitryptic power since it inhibited the action of trypsin. Vignes suggests that further studies on this organ would increase our understanding of the rôle of the phosphatides in metabolism. His conclusions have already been stated.

CONCLUSIONS

The brown multilocular adipose tissue, most commonly termed the hibernating gland, but known also by a variety of other terms, seems to be found mostly in rodents, but also in a few species of insectivora and chiroptera. A few similar cells are found occasionally in the perirenal fat of young children and newborn, but certainly there is no good evidence that the masses of fatty tissue described in other regions of the human body should be considered homologous to the hibernating gland of animals. It is not confined to hibernating mammals, nor is it present in all mammals that pass the winter largely in a dormant condition.

It is clearly evident that no one has gone extensively enough into the physiological significance of this brown multilocular adipose tissue to justify its classification as a gland. The granular character of the cytoplasm, the presence of numerous discrete fatty globules and other structural features of this tissue are not sufficient criteria by which to judge its glandular prop-

erties The prevailing opinion during the past 50 or 60 years has been that it is merely one type of adipose tissue The best designation for this tissue at the present time would seem to be multilocular adipose tissue

Its importance as a special source of food for the hibernating period has been overestimated, at least as far as bulk is concerned, yielding as it does only about one-thirtieth of the body tissues consumed in the case of the common European marmot (a slightly higher yield in the American marmot is indicated by figures to be published by the writer in the *Journal of Morphology*), and about one-fifteenth in the case of the hedgehog

Extirpation experiments are of little value on account of the extensive distribution of the tissue The effects of its extracts have been investigated practically by only a single worker (Vignes), who believes he has evidence from enzyme action that it functions as a protein sparer during winter sleep The latest theory, that it may be a special source of vitamins, is based on such meager data that it need not be taken seriously

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THE PRESENT POSITION OF TESTICLE TRANSPLANTATION IN SURGICAL PRACTICE A PRELIMINARY REPORT OF A NEW METHOD

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Much notoriety has recently been given in the lay press to the operation of testicular transplantation. This raises the question of the scientific aspect of the operation in general, hence it is desirable that the medical profession at large should have clear ideas as to its present status and what may be expected from it.

There are but very few cases of human testicular transplantation on record which have been followed by any durable degree of success. In fewer cases still has any scientific histological proof of the "taking" and vascularization of such a graft been given to substantiate claims that the graft was not resorbed. The value of such surgery must lie in the fact that a graft of this kind is able to live and function, and any method of transplantation must in the end be judged by this criterion. In the only case of human transplant reported by Lespinasse in 1913 (3) no such histologic proof was given, although it is stated that, clinically, sexual potency continued after the operation. A thorough search of the literature fails to disclose any other work done on human transplantation by Lespinasse.

Having for some years past been engaged in extensive experimental and clinical work connected with this question, I desire to bring its actual clinical status to notice, and to make a preliminary report on some of the results obtained.

A study of the extensive literature of this question since the first personal experiments of Brown-Séquard (1) shows that the testicle has a double secretion, that of the sperm cells proper, or seminiferous tubuli, and that of the interstitial glandular substance. The secretion of the seminiferous tubuli is concerned alone with fecundation, the interstitial glandular secretion has been clearly proved by a multitude of investigators to

be a hormone acting on the general system. This is a male sexual hormone, acting as a sex stimulant, and responsible for the development and maintenance of sex characters and desire.

The physiological findings naturally led to the investigation of methods having for their object the induction of the increment in individuals in which it was deficient. The best known of these methods is that of testicular grafting.

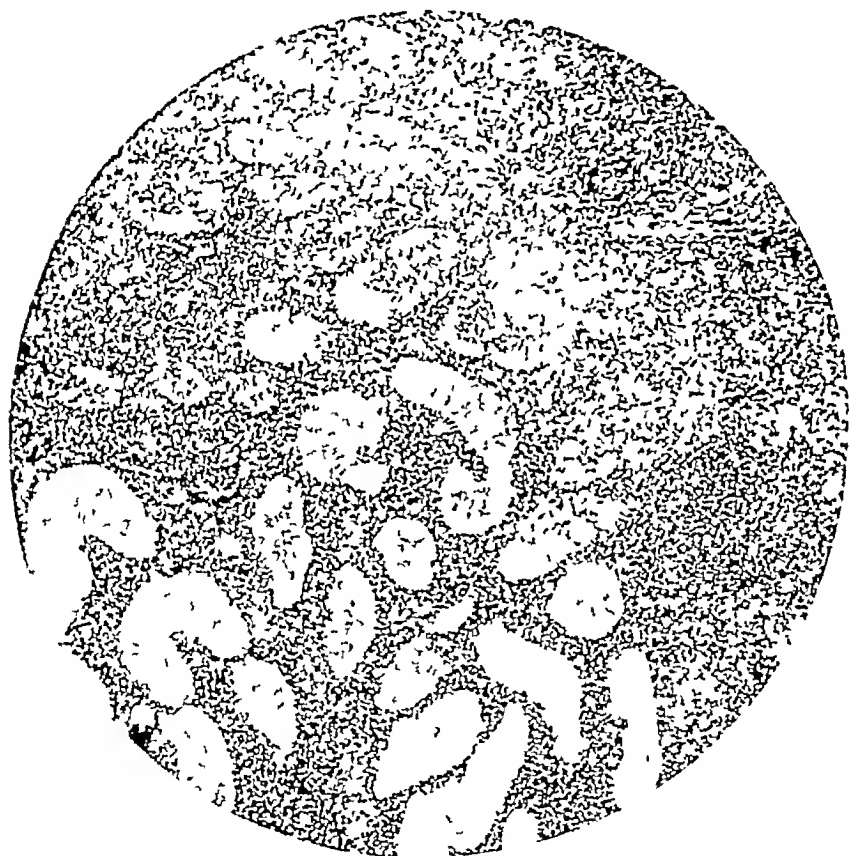


Fig 1 Photomicrograph Transplant of testis of higher ape into man. Author's technique. Magnification 60 diameters. Observe regression of tubuli seminiferi, proliferation of interstitium and vascularization. Removed four months after transplantation.

By numerous animal experiments it was established that either homo- or hetero-plastic grafting of testicles is possible in animals, that sometimes these grafts "took" and at other times they did not, the difference in results suggesting either a faulty technique or that some racial or specific incongruity rendered the "taking" of a heteroplastic graft impossible. The technical difficulties might be ascribed to difficulty of obtaining vasculariza-

tion in the transplanted tissue due to implantation in an unsuitable region or to an unsuitable method or to both

The homo- and hetero-graft experiments in animals, supplemented by histological findings, reported in 1919 by Professor Serge Voronoff (2) of Paris (with whom it has been my privilege to collaborate for some years) undoubtedly gave the most brilliant results and proved that transplantation of animal testicular tissue from young to old animals of the same species was followed by viability and could be followed by clinically demonstrable renewal of physical and sexual vigor and sexual impulse which had become lost

Although various clinical attempts have been made to transplant testicles from man to man the operation can be said to have been only partially successful. In many cases the graft was expelled after a short time and in others it became absorbed after a greater or less interval. It has been generally believed that in the cases where a graft has been retained that it exerted a hormonal influence and that physical well-being and sexual potency was for a while restored. In but few cases, however, was the actual "taking" of the graft verified by histological findings

From the study of the literature and especially after visiting the clinics of Voronoff in Europe, I was convinced that the operation of testicular transplantation could be made a practical surgical procedure

The difficulty of vascularization could, I believe, be met by a suitable site and method of implanting the graft. The great difficulty, however, of obtaining perfectly suitable material was not one easily solved, as for obvious reasons human testicular material is difficult to obtain, and is not always likely to be free from disease and suitable for transplanting

By a series of experimental investigations I devised a method of transplantation which I call the "lantern" technique which has given perfectly satisfactory results as regards the "taking" and rapid vascularization of testicular grafts. I have also succeeded in successfully transplanting the testicles of higher apes to man and have obtained results which are in every way analogous to those obtained in transplantation of human testicles

Moreover, these transplants of the higher apes have been removed after several months and proved histologically to be in full activity and vascularized. This is the first time that successful transplantation from ape to man has been verified by histological proof.

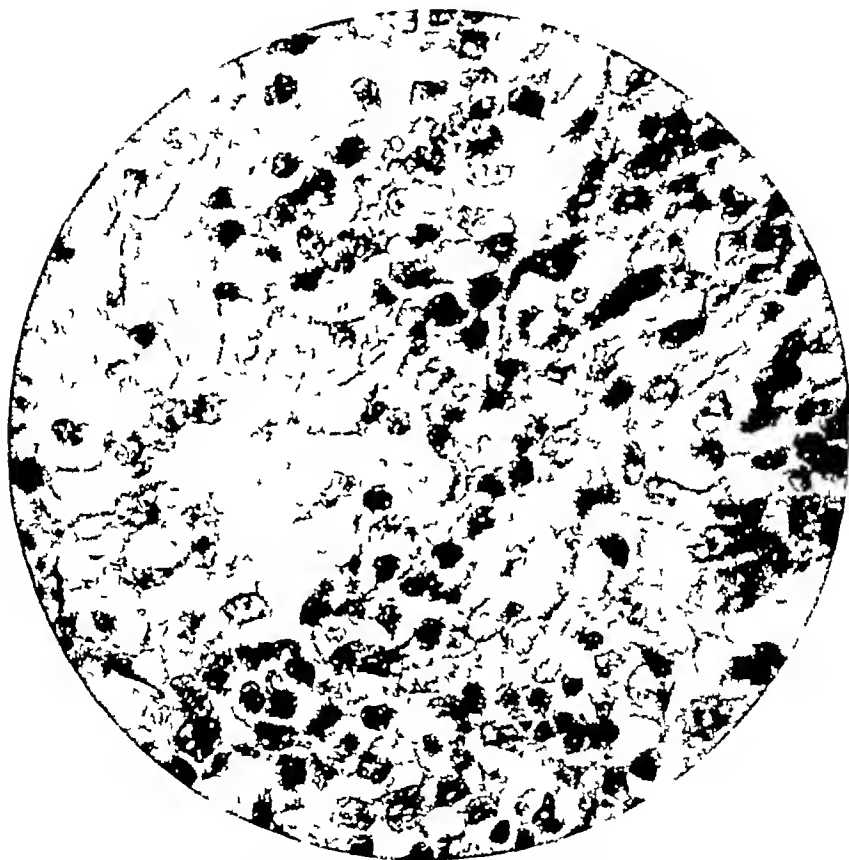


Fig. 2 Same as Fig. 1 Magnification 560 diameters. Observe what appear to be Leydig cells, giant cells and abundance of cell life in well nourished area.

The accompanying illustration is a reproduction of the histological appearance of a section from such a graft which was removed four months after implantation. It shows regression of the seminiferous tubules, proliferation of the interstitial elements of the testicle and vascularization of the graft.

I have done a great many transplantations from the higher apes to human subjects and in the cases where I have employed the improved technique almost invariably excellent results have been obtained.

The full details of my surgical technique and clinical findings will be published later in a more complete report

SUMMARY

A new technique has been devised whereby it has proved possible to transplant testes from man to man or from higher ape to man and secure persistence of the graft with consequent clinical improvement of symptoms due to gonadal deficiency. Two photomicrographs are reproduced, showing persistence of graft

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THE STEINACH OPERATION REPORT OF 22 CASES WITH ENDOCRINE INTERPRETATION

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The ligation of the ductus deferens combined with vasectomy has become now generally known as the "Steinach operation." By its effects, I am inclined to designate it as "endocrine surgery." I shall assume that the theory on which Steinach based his practice is fairly well known, and discuss it only very briefly, referring to my other publications for more detailed information †

In the 22 cases herewith presented unilateral ligation under local anaesthesia was the rule. The vas was carefully isolated and separated from all accompanying structures for a distance of about 2 cm. Two heavy silk ligatures were placed around the vas, about 2 cm. apart. The one nearer to the testicle was reinforced by a fine silk ligature in order to use it later for sewing the lower stump into the tissue near the upper corner of the wound, for the purpose of suspension. Before this was done, a short piece of the vas between the heavy ligatures was resected. The tunica vaginalis and the skin were closed with catgut. The principle of the procedure is to close the vas, prevent re-communication of the stumps, and preserve the blood supply.

In a few cases I have observed irritation, and in two, even sloughing out of the silk without actual infection. Chromic catgut was therefore used in three cases, but Steinach and his surgeon strongly advise the use of silk, as it excludes the possibility of a re-opening of the vas. I am personally now using nothing else, but insist on double sterilization of the silk.

The place of the incision varied. I have either exposed the vas near the root of the penis or incised the scrotum and ligated near the epididymis. A somewhat quicker result can perhaps be looked for after the latter procedure. I have nowhere ligated between epididymis and testis.

†N. York M. J. [etc.], 1922, 114, 687, *Ibid.*, 1922, 116, 203, *Am. Med.*, 1922, 28, 435.

According to Stemach's theory, ligation of the vas (not vasectomy alone) causes through back-pressure and later inactivity an atrophy of the generative portion of the testis, with subsequent proliferation of the so-called puberty-gland, consisting mainly of the interstitial (Leydig) cells. The increased formation of gonadal hormone re-activates the entire endocrine system of the patient, causing clinical results, varying from nothing more than an "endocrine tonic" to an almost actual "re-juvenation."

As an indication for the operation,—speaking generally and from an endocrine point of view—I have taken a hypofunction of the gonads, or better, an inferiority in the gonadal activity. I have assumed that "senility" is due to a naturally occurring, i. e., an acquired hypo-gonadism (primarily or secondarily) with an accompanying dysfunction of the rest of thecretory organs. If this state of affairs exists at a relatively early stage of life, I speak of "premature senility." Here, congenital inferiority of the gonads or the whole endocrine system plays perhaps a rôle. Such endocrine constitutional inferiority, or weakness of the gonads I also assumed in certain cases of sexual impotence (those of gonadal origin). Here the other endocrine organs are not affected in the same sense, and no symptoms of general senility are apparent. Those cases have also been described as "partial senility" and "partial premature senility," by Schmidt.

The principal contra-indications were Advanced senility with atrophic testes, and a seriously impaired cardio-vascular apparatus. I have also refused the operation where it seemed that other therapeutic procedures, for instance, rest, should first be tried for symptoms of senility and where evidence of organic defects, like tabes, existed, to explain sexual impotence.

The important questions arise: Where can we expect fairly good results, where excellent ones, in what cases none at all, and can harm be done in ligating a man's vas, causing him to form a new puberty gland? The last question I am inclined to answer with "No." We have no proof whatever of any injurious effects, all the evidence pointing to the harmlessness of the procedure. Even where additional gonadal hormone is not required, we can trust in the balancing power of the endocrine apparatus as a whole. To the other questions I cannot give a definite answer,

but would like to suggest a way of examination and classification which may in the future, and based on larger clinical material, enable us to understand more clearly the endocrinological consequences of the vasoligation, and thus differentiate favorable from unfavorable cases. I have therefore attempted to classify all cases according to their endocrinological "constitution," taking into consideration their life history, the character of their complaints, and their physical make-up. I have designated them as "thyroidal," "gonadal," etc., and where two glands seemed to be prominent in the patient's constitution, I described them as "thyro-gonadal," "pituito-adrenal," etc., putting the one most likely primarily delinquent in the first place. I have not differentiated between "hypo" and "hyper," unless this was glaringly justified.

I have interpreted the patient's symptoms from an endocrine point of view as far as possible, and likewise the changes that appeared after the operation. Then, taking the patient's constitution into consideration, I have sought to answer the question which constitution offers the best chances and in the sphere of which gland the principal changes might develop. This means clinically: Which are the favorable cases, and what will happen to them after the operation?

In view of the modernity of endocrine studies, a divergence of opinion might naturally arise regarding the classification of the constitution and the interpretation of symptoms. The study of more data is therefore imperative.*

The complaints of the senile cases were of the usual nature, partly mental and partly physical, and need not be described in detail.

The age in the 22 cases reported lay between 36 and 64. They consist of (1) 12 cases of senility including premature and physiological old age (acquired gonadal deficiency), (2) 8 cases of congenital inferiority of gonads (hypogonadism) with sexual impotence, (3) 1 case of dyshormonism (No. 9), (4) 1 case of carcinoma.

Cases 1 to 8 have already been reported elsewhere with clinical details, as previously stated, but at that time I had not touched upon the endocrine aspect.

*It seems fair to state that my endocrine interpretations are based on the plan originated by Dr. Joseph Frankel.

Regarding results, it must be noted that it sometimes takes six months, perhaps even more, for the full quota of clinical effects to develop. Positive improvements within this period give no definite clue as to their final intensity. I have found it practical to classify the results as follows: (1) *Negative*, if no changes at all occurred attributable to the operation, after a period of six months or more, (2) *Subjectively positive and doubtful*, if the patient stated improvements in his subjective sphere only, doubtful regarding endocrine interpretation. These cases have naturally a limited value as scientific evidence, and (3) *Positive*, if clear evidence, for instance objectively, of a beneficial effect was at hand, in some cases naturally only "partial."

ENDOCRINE OBSERVATIONS AND FURTHER STUDY OF EIGHT CASES, PREVIOUSLY REPORTED

CASE 1 CLERK—58 YEARS

Diagnosis Premature senility with mental depression and varicocele

Constitution Adreno-gonadal

Operation February 2, 1921, in combination with varicocele (Dr. Reitzfeld). This patient did not know that the Steinach operation was performed.

Last Examination (Dr. Reitzfeld, five months p. o.) Distinct mental and physical improvement, gain in weight of twelve pounds, no change in sexual life, no endocrine study was attempted.

Result Positive (auto-suggestion excluded)

CASE 2 MERCHANT—57 YEARS

Diagnosis Premature senility, chronic arthritis in both knees

Constitution Pituitary-gonadal

Operation November 1, 1921

Last Examination (seven weeks p. o.) Marked functional improvement in his knees, general condition decidedly improved, sexual power increased, a distinct thyro-pituitary-gonadal influence apparently manifest, but the time of observation too short to draw reliable conclusions.

Result Subjectively positive (Doubtful)

CASE 3 COLLEGE PROFESSOR—55 YEARS

Diagnosis Premature senility, prostatic hypertrophy with frequent micturition, affection of the internal ear (sclerosis) with increasing deafness.

Constitution Pituitary-gonadal

Operation December 28, 1921

Last Examination (seven months p. o.) Marked improvement in every way, hearing much better as proved by objective methods (Dr. Max Heimann), prostate smaller, urination normal, weight increased by six pounds, blood pressure constantly somewhat lower, within normal limits, sex-life unchanged.

Endocrine interpretation is doubtful, thyroidal and pituitary activity is improved. The effect in the gonadal sphere seems to have influenced the prostate only. For the libido the cortex cerebri is too

important and perhaps only influenced by the gonads when psychic factors are favorable This was not the case here

Result Positive

CASE 4 MANUFACTURER—48 YEARS

Diagnosis Premature senility, marked sexual impotence (not improved by transplantation of human (?) testicle or any other treatment)

Constitution Adreno-gonadal

Operation February 15, 1922 (ligature had possibly sloughed out)

Last Examination (four months p o) General improvement physically and mentally, gain in weight ten pounds at least, sexual ability decidedly better but not yet normal, nightly emissions occurred first time in several years, increase in libido very doubtful

Thyro-adreno-gonadal influence is apparent, but only in a moderate degree

Result Partially positive

CASE 5 LABORER—38 YEARS

Diagnosis Premature senility with sexual impotence, varicocele

Constitution Thyro-adrenal

Operation February 20, 1922

Last Examination (March 30, 1922) No definite changes

Result Patient could not be reached for re-examination, negative, six weeks p o Case not classified

CASE 6 CONTRACTOR—58 YEARS

Diagnosis Senility (premature)

Constitution Adrenal

Operation February 28, 1922

Last Examination (August 18, 1922, 5½ months p o) Marked improvement, more ambition and no more mental depression, gain of about six pounds in weight, appearance much better, complexion markedly improved, former frequent urination normal

Patient says that he perspires more freely than in former years, and also noticed a stronger growth of his beard, as evidenced by necessity of more frequent shaving His blood pressure (syst) was around 180, is now 150 Pulse pressure has decreased from 85 to 75 His prostate showed a distinct hypertrophy, especially of the left lobe It is still large, but both lobes alike, the left one having decreased in size The skin reaction has changed from faintly red with white borders to a distinct red line of long standing He feels perfectly able to resume business responsibilities which he had dropped for years Sex desire and ability has increased little if any

Here the changes in perspiration, complexion, growth of beard, blood-pressure and skin reaction indicate increased thyroid activity, balancing the (constitutional) adrenal dysfunction, as evidenced by blood pressure and skin reaction (Sergeant line)

Result Strongly positive

CASE 7 WATCHMAKER—36 YEARS

Diagnosis Sexual impotence for the last nine years, premature senility

Constitution Gonadal

Operation March 6, 1922

Last Examination (August 16, 1922, 5½ months p o) Decided mental and physical improvement, patient has returned to work that he had discontinued for many months, feels as well and ambitious as ever, more self-assurance, acne on back disappeared

The patient volunteered two interesting statements First, he

had been using a 2½-inch focus magnifying glass for his work which he finds too strong now, is using a 3½-inch focus now, second, has to shave every day compared with every two to three days formerly, he claims that his hair is growing "awfully fast" Sexual impotence is practically cured and he has had sexual intercourse satisfactorily for the first time in the last 9 years He intends to get married
Here also the thyroidal stimulation is evident, in addition to the increased gonadal activity in accordance with his constitution
Result Strongly positive

CASE 8 EDITOR—58 YEARS
Diagnosis Premature senility
Constitution Pituitary-adrenal
Operation March 15, 1922
Last Examination (August 18, 1922, 5 months p o) All physical and mental complaints have completely disappeared, especially his frequent (pituitary) headaches, enjoys perfect health, skin reaction has changed from red with white borders to distinctly red, (syst) blood and pulse-pressure have dropped 10 mm within normal limit; sexual limitations are unchanged
In accordance with the patient's constitution the balancing of the pituitary and adrenal dysfunction is very evident. This patient is a highly intelligent and critical man No change in the gonadal sphere is apparent
Result Positive (except sexually)
For additional details as to symptoms and other clinical data of the above eight cases, I wish to refer to my previous publication of August 31st, 1922, in "Am Med "

PRELIMINARY REPORT OF 14 ADDITIONAL CASES

CASE 9 ENGINEER—36 YEARS (REFERRED BY DRS D M KAPLAN AND GREG STRAGNELL)

Principal Complaints and Symptoms Patient feels physically and mentally "inferior", has frequent (pituitary) headaches and digestive disturbances, suffers from premature ejaculation and partial sexual impotence

Diagnosis Dyspituitarism with secondary dysgonadism, gigantism, varicocele, scoliosis, chronic otitis media with moderate deafness

Constitution Pituitary
Operation March 17, 1922, in combination with partial resection of the varicocele (the Stenach operation was performed as an attempt to influence the endocrine system), a part of the silk ligature sloughed out without infection

Last Examination (3½ months p o) After "ups and downs" doubtful as to resulting from operation, the patient now states that his headaches have decidedly improved in that they are less frequent and less intense, better digestion, sex desire irregular but more frequent nightly emissions, no opportunity to test his potency, no frequent changes in weight, blood pressure, etc
Result Doubtful, subjectively positive (although the improvement suggests an influence on his constitutionally inferior pituitary)

CASE 10 DENTIST—39 YEARS (REFERRED BY DR STRIKLER OF PHILADELPHIA)

Principal Complaints and Symptoms Sexual weakness began four years ago, now complete impotence, 25 years ago contracted syphilis that was treated until several Wassermann examinations of blood and one of spinal fluid were negative, knee jerks distinctly exaggerated, otherwise physical examination negative

Diagnosis Impotentia sexualis somatica, psoriasis, lues (cured?)

Constitution Adrenal

Operation March 17, 1922

Report by letter No change (2½ months p o)

Result So far negative

CASE 11 AGENT—56 YEARS

Principal Complaints and Symptoms Fifteen years ago one kidney removed on account of stones, frequent attacks of dizziness, poor memory and lack of ambition, slight deafness, glycosuria, disappearing after a few days of strict diet

Blood Pressure (Syst) between 160 and 170, pulse pressure between 60 and 80, weight, 138 pounds, no skin reaction, sex desire and ability gradually waning, prostate enlarged, occasional slight attacks of gout, irritable and depressed

Diagnosis Premature senility, beginning arteriosclerosis, diabetes mellitus

Constitution Thyro-adrenal

Operation March 27, 1922 (Healing of wound delayed)

Last Examination (4½ months p o) In the intervening time there were "ups and downs" in patient's subjective complaints, no improvement in his sugar tolerance and in his sexual limitation apparent, indigestion, probably due to his lack of teeth and inability to masticate properly, less depressed and somewhat more ambition, generally livelier, looks better and hears better as noticed by his relatives, his skin reaction, faintly red, his weight slightly increased (140 pounds), his attacks of dizziness practically ceased since about 4 weeks p o, his blood pressure dropped and now changes between 130 and 145, syst, pulse pressure between 45 and 55

So far only slight stimulation of thyroidal activity seems to manifest itself, with subsequent effect on the adrenals

Patient's improved hearing has been confirmed through objective methods by an ear specialist (Dr Max Heimann)

Result Partially positive

CASE 12 NAVAL OFFICER—53 YEARS

Diagnosis Beginning arteriosclerosis, angina pectoris

Constitution Adreno-gonadal

Principal Symptoms and Complaints Mild but frequent attacks in heart region, radiating into left arm, occasionally quite severe, blood pressure, systolic, 155, diastolic, 110, pulse, 76

X-ray examination of heart showed moderate enlargement of heart and aorta, weight 161½ pounds, sexual ability decreasing, prostate enlarged

Operation April 11, 1922, one month after the operation the subjective condition was about the same, but patient noticed stronger erections, his blood pressure, systolic, 135, diastolic, 90, weight, 163 pounds, otherwise no change

Case not classified

CASE 13 IMPORTER—43 YEARS

Diagnosis Hypo-gonadism, sexual weakness

Constitution Gonado-pituitary

Principal Complaints and Symptoms Patient feels that through his sexual inferiority (weak desire as well as limited potency) he "is losing something in life", desires marriage, fears premature senility

Operation April 21, 1922 (ligation with chromic catgut)

Although no re-examination has been possible, the patient reported (5 months after operation) that no noticeable changes have occurred

in his condition He is in excellent health, physically and mentally I am, however, inclined to classify his case as

Result So far negative

CASE 14 DENTIST—53 YEARS

Diagnosis Premature senility, beginning arteriosclerosis, impotentia sexualis, doubtful syphilitic history

Constitution Adrenal-gonadal

Principal Symptoms and Complaints Nervous twitchings, insomnia, increasing weakness of sight and hearing, lack of "pep", shortness of breath on exertion, sexual impotence for the last 10 years, x-ray examination of heart (Dr Philips) shows a moderate general hypertrophy without insufficiency or dilation, blood pressure, systolic, around 140, pulse pressure, 60, pulse, 76-80, weight, 155½ pounds

Operation April 29, 1922 (ligated bilaterally with chromic catgut)

Examination (one month p o) Patient claims to have more energy and ambition, but only since a few days, also distinctly better erections, but no intercourse attempted, blood pressure, systolic, 122, pulse pressure, 37, pulse, 64, weight, 159½ pounds (4-pound gain) In a letter of July 31st from out of town, patient reported to be in about the same condition as on the last examination

So far an influence on the adrenals and in the gonadal sphere is evident Although objective changes seem to have occurred, the time of observation was too short to call the result so far other than doubtful

Result Doubtful

CASE 15 MERCHANT—63 YEARS

Diagnosis Beginning senility

Constitution Pituita-gonadal

Principal Symptoms and Complaints Patient feels that oncoming of age interferes with his ability to work, especially in regard to memory, ambition, power of concentration, etc., blood pressure, systolic, 138, pulse pressure, 58, prostate enlarged

Operation May 3, 1922 (ligation with chromic catgut) (Traumatic non-infectious epididymitis followed, but healed promptly)

A letter of August 5th (three months p o) reads in part "I am feeling fine since the operation There has been a general improvement in my health, particularly the prostate trouble I have gained some flesh I cannot see that my sex powers have increased to any extent."

(No endocrine interpretation attempted from written reports)

Case not classified

CASE 16 ELECTRICIAN—39 YEARS

Diagnosis Premature senility, sexual impotence

Constitution Thyro-gonadal

Principal Symptoms and Complaints Mentally depressed, cannot keep a good position through lack of ambition, premature ejaculation amounting to sexual impotence that depresses him greatly, looks almost senile—about 15 years older than his age, organic mitral heart lesion well compensated, blood pressure, systolic, 142, pulse pressure, 32, weight, 136 pounds

Operation May 26, 1922

Examination June 5, 1922 Blood pressure, systolic, 115; pulse pressure, 30, weight, 137¼, no change of subjective symptoms

Since no further report has been received of this patient, his case has not been classified

6 were not classified, since no report was received about their condition. The results, therefore, can only be judged in 16 cases. Of these, I consider 9 positive (more or less strongly), 4 doubtful or subjectively positive, 3 negative. The doubtful and negative cases may have to be judged differently after longer observation.

Regarding the endocrine manifestations, I would like to summarize my observations as follows, giving a theory more than scientific facts.

The most frequent and most prominent clinical manifestations as the result of the new activity of the puberty glands seem to be due to increased thyroid activity.

Outside of the thyroid, the re-activated puberty gland seems to influence essentially those glands that are most prominent or delinquent in the patient's constitution.

Distinct changes in the gonadal sphere appeared mostly in patients with a gonadal or partly gonadal constitution. Therefore, the claim of certain German investigators that the increase of sexual activity was *regularly* observed could not be fully substantiated.

The following, however, must be considered as well established scientific facts, also deduced from the above observations.

The Steinach operation increases the activity of the puberty gland. This re-activation has an influence on the endocrine system in the sense of stimulation, regeneration, and restoration of equilibrium. No injurious effects have been observed.

Regarding prognosis, I can at present express only a very vague opinion that gonadal or partly gonadal constitution seem to be most promising. I believe that a further close observation of the treated cases from an endocrine point of view will greatly enhance our knowledge of the inter-relationship of the different glands, especially the inter-relationship of the gonads with the rest of the endocrines.

AN ANALYSIS OF ONE THOUSAND TESTICULAR SUBSTANCE IMPLANTATIONS

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In presenting this phase of the study of internal secretions, one cannot be unmindful of the publicity which has been given the so-called interstitial gland during the past three years, and of the bad impression this has made upon the medical world

The rather doubting, skeptical—even intolerant—attitude of the medical profession toward a subject which has been so largely flouted before the public by newspapers, eager for sensational discoveries, particularly along sex lines, can well be condoned

In the past, physicians have had their fill of the "lost manhood" charlatans. And when word came from abroad in 1918 that youth could be renewed and many of the potentialities restored by the engrafting of interstitial glands of the monkey, the medical profession for the most part ridiculed it, feeling that it was similar in purpose and intent to the widely heralded tuberculosis cure with turtle serum coming from Germany in 1913

The public, however, clamored for more news about this wonderful and all-absorbing topic, with its mystery and sex-appeal. It became a very interesting subject of conversation among men as well as women in all walks of life

Soon after Voronoff brought forth this monkey gland announcement, it was emphasized that Lydston of Chicago had been doing similar work with human material since 1913, and that the medical department of the California State Prison had following his example, been transplanting testicles from recently executed convicts to senile and devitalized men for some time

Brown-Séquard, in experimenting on himself in 1889, found that by injecting an extract derived from the testicles of dogs, definite dynamic effects were produced. He regained much of his former strength, fatigued less easily, and was able to do work greatly in excess of what he had been capable of before. His

mental faculties were increased, and intellectual efforts became easier. He noticed that he was greatly relieved of constipation, and believed that the testicular extract had an influence, particularly on the spinal cord.

Because of the activities of quacks and charlatans in the time of Brown-Séquard, the complete investigations of this extract were not fully carried out as they should have been. With his experiments, however, an interest in the study of internal secretions was aroused. Indeed, this work marks the "birthday of endocrinology," as such.

This paper deals with one thousand injections of animal testicular substance into 656 human beings. The greater number received only one injection, while to some were administered as many as seven. Among the patients treated were ninety-six unconfined people, including thirteen physicians and seven females. The remaining five hundred and fifty were inmates of the state's prison. This does not include the twenty cases in which human testicles were transplanted from executed convicts to others. But it does include about ninety cases in which a piece of ram's testicle the size of a dollar was implanted by operation into the scrotum or abdominal wall.

It was found that these heterogenous grafts were gradually absorbed. In order to obviate operation in which the rectus fascia of the abdomen was exposed and an implant inserted, a syringe method of implantation was devised. Immediately after the death of the animal, the scrotum with the testicles enclosed was tied off and cut away. This was then taken to the operating room, where the external hair or wool was clipped off and the skin painted with iodine. It was then incised longitudinally, and the cut edges retracted and held away with haemostats. Using other scissors and sterile clamps, the next of the many coats of the dartos fascia were likewise opened, until the tunica vaginalis was reached. The tunica was in like manner incised and retracted, revealing the perfectly aseptic testicle enclosed. This was seized with a tenaculum and withdrawn entirely free of contamination. The epididymis and surrounding tissues were then cut away.

The testicular substance was cut into strips with a knife or cork-borer in sizes suitable for the filling of the pressure syringe. This instrument is similar to the one devised by Beck for paraffin

injection A dental syringe with a No 16 needle, $3\frac{1}{2}$ inches long, has been found to be satisfactory

By this means the semi-solid testicular substance was injected by force underneath the skin of the abdomen With this method there were comparatively few sloughs, and the patient was not subjected to a week's hospital inconvenience

The testicles of goats, rams, boars and deer have been used So far as can be determined there is very little difference in the effects produced by testicular material obtained from various animals

The first of these cases was treated in January, 1920, and the last in February, 1922

In order to see if there were any therapeutic value in this procedure, and if possible to determine what cases, if any, might be benefited, anyone who applied was given treatment The matter was fully explained to the patient, and he was allowed to use his own judgment as to whether he cared to submit or not

It was probably fortunate that this work could be carried out in a prison, for in such a place all men are treated alike, and live under the same conditions of food, work, and general surroundings A good opportunity was given for observing the results, because the patients could be under daily observation, and the "follow-up" conditions were ideal

As soon as a new prisoner is received at San Quentin, he is given a thorough physical examination, so that his status at entrance is well known Any changes taking place in the condition of the prisoner can be easily checked up

In starting this analysis, it might be said that eleven of the patients are now dead One is thought to have committed suicide, one died of uraemia, three of pneumonia, and six succumbed to tuberculosis

From a compilation and study of data from these 1000 treatments, it is believed that testicular substances do have a decided effect on conditions of general asthenia This term is applied to patients who are underweight, lack energy, sleep poorly, have scant appetite, and, to use their own expression, are "all run down" With them nothing definitely pathological can be found Usually within the first week after the treatment they gain in weight, have increased appetite, enjoy their work, and evince a general buoyancy Of the 326 patients so diagnosed,

305 have shown by their actions, by their weight, and by their own written reports that they have been markedly benefited. None who have been so afflicted and have received the treatment became worse, but a few did not improve.

In the early experimentation, it was thought that the goal to be reached, and the proof of the treatment, was sexual stimulation. Usually with a relief from an asthenic condition, the sexual manifestations appear as the patient regains normality. If his general condition is below par, his sexual desires may be somewhat lethargic.

Of the total number of patients, 81 reported increased sexual stimulation. This was evidenced to them by frequent erotic dreams with emissions, and frequent erections without undue sexual cause.

It can hardly be said that this treatment cures impotency, although some who have not had sexual manifestations for years have a renewal of this function. On the other hand, three men who claim that they were normal sexually before the testicular substance injections report that their potentialities in this respect have almost entirely faded away.

The difficult problem in this investigation, as in any other regarding health, is to know just how much reliance can be placed in the patient's own statements and observations.

Prisoners as a rule are antagonistic, that is, they are against the officials who have anything to do with their incarceration. The state put them in prison—they are against the state. The officials represent the state—hence they are against the officials. This is mentioned merely to show that anything done by officers of the medical department, or any other department in the prison, would be harshly criticised by them if no benefit were derived from it.

With the gland treatment, however, most of those who took it give a fair and truthful report as nearly as can be determined.

After a few of the men had undergone the injection and found that there was little pain to it, and that they were benefited, they told the other inmates and as a result there were many applications. Instead of being against the treatment, they were for it, even overcoming their natural tendency to oppose.

One of the skin diseases most resistant to treatment is acne. This affection frequently comes at that transition period, when

the youth is entering manhood. Usually after several years it disappears. Among the 656 patients treated with testicular substance, 66 had this disease.

It can be said that acne is markedly influenced by this treatment. One does not have to rely upon the statement of the patient in this regard, for the improvement in the face can be seen. Photographs have been taken before and after the implantation. The acne does not dry up as if by magic, but the number of pimples decrease and very few comedones appear when they are once removed.

Whether testicular substance contains some inherent power like adrenalin to influence asthma, or whether by means of a hormone sent into the blood stream, acting upon the adrenal glands, adrenalin is elaborated, and thus alleviates asthma, is not known. But of the 21 patients of this series who suffered from asthma, 18 secured relief or had the severity of their attacks greatly decreased.

One man, aged 23, who had had asthma all his life, has been given four injections at intervals of three or four months. His arms were badly pocked where he had taken adrenalin by hypodermic. At the present time he rarely has an asthmatic attack. Others give somewhat similar histories. Three of the asthmatic patients have had no relief.

In asthma, as in all other conditions treated, it has been found that sometimes one injection of a dram of testicular substance does not have an appreciable effect. A subsequent injection may, however, prove of benefit. This may be due to the presence or absence of some body in the testicles of one animal that is not in another. This of course is only conjecture.

In some patients the substance injected will remain under the skin and be plainly felt as a shot-like body for several months, while in others it disappears within a few weeks.

The possible advantage of using the whole testicular substance, instead of the extract as Brown-Séquard did, is that it is absorbed so slowly that in this process of absorption the hormone is gradually given off, producing a continuous effect. The extract may be absorbed within a few hours.

There were four cases of diabetes. Three of these claimed improvement, in that they gained in weight and improved in general condition. One man, aged 67, had had diabetes for nine

years, his urine was full of sugar, and there was some gangrene of his toes. He was given two treatments of testicular substance in February and May of 1921. In October he was transferred to Folsom prison, where Dr. Clattenburg, the resident physician, reported that, although this man partook very freely of Christmas candy and pastry, he was unable to find any sugar in the urine after repeated tests.

Three subjects having locomotor ataxia claim that the pains were lessened and that they felt better. Of course, the disease was in no way arrested. It seems that in some way this therapeutic agent has some influence in pain.

Fifty-eight of the patients treated complained of rheumatism. By this term is meant those pains in the back, shoulder and legs for which no definite cause can be found. Forty-nine claimed that their pains have stopped, while four found no difference, and five reported their condition slightly worse. In this connection it might be said that several affirm that cramps in their legs have disappeared.

Among the patients treated, thirty-four were senile. Twenty-seven of them showed improvement in that they were more energetic, ate better, and showed more activity mentally and physically. The observations made on these old men were in many respects similar to those which Brown-Séquard made on himself.

The results in tuberculosis have not been particularly encouraging, for, as previously stated, six of the seventeen patients so afflicted died. Of the others, 10 are benefited by increase in weight and appetite. Those who died were in advanced stages of the disease. One woman with pulmonary lesions gained fifteen pounds, and in spite of afterward contracting influenza, subsequently gained two pounds additional.

Fifty-six patients were suffering from neurasthenia. Some of them were the "hospital pests," never benefited by anything. Of this number, however, thirty-three cases showed decided improvement. They gained in weight, felt fine, and apparently forgot many of their fancied ailments.

It has often been asked what part psychology plays in this treatment. To be sure, that is to be thought of. But it can hardly be said that psychology will influence asthma, or benefit acne, or, without other stimulation, spur up the sexually dor-

ment The marked improvement in the general asthenic cannot well be placed at the door of psychology

All of the thirteen physicians who took the treatment, with the exception of one reported good results It is extremely doubtful whether auto-suggestion entered into their case

In their reports, many of the patients claimed that they have been relieved of constipation No data has been kept on this phase of the subject Nor have any data been compiled, in these experiments, on blood pressure

Forty-one of those treated complained of poor vision which necessitated glasses Thirty-two report that their vision was greatly strengthened after the implantation One man, an official of the prison, declares that before his treatment he had difficulty in distinguishing the torpedo boats which ply up and down the bay Following two injections, he affirms that he is not only able to distinguish the boats, but he can read the numbers on the bow In addition, this man has gained forty pounds in weight He is an accountant, and credence should be given his statement

An endeavor was made to interest oculists in this matter of eye improvement The work was taken up but was not finished

There have been found no ill effects resulting from the testicular substance implantations, other than an occasional slough of the material In those cases which do slough, the site of injections swells, becomes reddened and slightly painful An incision brings out necrotic material and leucocytes After a few days this heals over with no great inconvenience

Four subjects have had edema of the scrotum within a few days after the injection This soon subsided There are no bad constitutional effects such as fever, chills pains or headache The patient goes about his work as usual although he might feel some soreness, and occasionally an itching sensation near the needle wound

In conclusion it might be said that investigation of this subject is being kept up in the endeavor to seek the truth Many obstacles are placed in the way and the bad impression which is engendered through publicity and the unwarranted claims of medical buccaneers on this poorly charted sea of research must be overcome

SUMMARY

The results of 1000 implantations of testicular substance in 656 human subjects, including 7 females, are reported. Striking objective improvement was seen in numerous cases of general asthenia, acne vulgaris, asthma and senility. Subjective or objective improvement was seen in various cases of rheumatism, neurasthenia, poor vision and a few other conditions. The results as a whole are tabulated. In general testicular substance seems often to have a beneficial effect in relieving pain of obscure origin and promotion of bodily well being. The operation is practically painless and harmless.

ANALYSIS OF CASES

	TOTAL CASES	BENEFITED	NOT BENEFITED
General asthenia	336	305	31
Rheumatism	58	49	9
Acne vulgaris	66	54	12
Neurasthenia	56	33	23
Poor vision	41	32	9
Asthma	21	18	3
Tuberculosis	17	10	7
Senility	34	27	7
Sex lassitude	95	81	14
Impotence	19	12	7
Psychopathic inferiority	8		8
Epilepsy	5	3	2
Dementia præcox	8	1	7
Paranoia	3	2	1
Diabetes	4	3	1
Locomotor-ataxia	3	3	
Drug addicts	32		
Dead	11		
Unclassified	28		
No report	30		

CONCERNING THE PATHOGENESIS OF THYROTOXICOSIS PART II

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THE DYSTHYROIDISM OR DYSFUNCTIONAL THEORY

In the preceding section of this article, published in the September issue, the various theories of the pathogenesis of exophthalmic goiter were summarized and critically considered. In particular, evidence was offered that the common conception of Graves' disease as due merely to "hyperthyroidism" is untenable. In the succeeding paragraphs evidence will be adduced that the disease represents not "hyperthyroidism" but dysthyroidism.

If we accept that the neurogenous and hyperthyroidism theories are untenable, it must still be borne in mind that the source of the clinical phenomena of Graves' disease lies unquestionably in the thyroid gland itself, no matter whether the ultimate, morbid stimulus originates without or within the gland or both. Objectively considered, there remains then but one other possible explanation for the symptoms and signs of this clinical disorder, namely, that they are the result of an *abnormal* metabolism of the thyroid gland, *i e*, a *dysfunctional* condition. This is at direct variance with the conception of primary hyperplasia, an accelerated normal metabolism and a hyperfunctional condition of the gland. The dysthyroidism theory accepts a "qualitatively altered secretion" as responsible for the general symptoms and signs of the disease. Among those supporting this view are some of the closest students of Graves' disease: Oswald, Minnich, Murray, von Leube, Howard, West, Dock, Marine and Lenhart, and McCarrison. The dysthyroidism theory is based upon etiologic, pathologic, metabolic and clinical data which now follow in detail.

ETIOLOGIC DATA SUPPORTING THE DYSTHYROIDISM THEORY

As is well known, thyrotoxicosis is liable to occur in families showing a tendency to goiter and hypothyroidism. In indi-

viduals of the same family, certain members may exhibit thyrotoxicosis, others hypothyroidism. A mother with myxedema, reported by Maude, bore two children, both of whom later developed Graves' disease. Murray and other writers cite similar instances. The familial occurrence would bespeak a common origin and etiologic relationship of the two clinical conditions.

The etiologic relationship of goiter to Graves' disease is important. According to the brilliant researches of Marine and Lenhart, and also Gaylord, on thyroid hyperplasia, adenomatous goiters may be properly regarded as caused by toxic or other agents inducing primary cellular injury or exhaustion followed by secondary hyperplasia. (See succeeding section.) That thyrotoxicosis is likely to develop in such instances has been shown by Wilson, Plummer and Boothby of the Mayo Clinic. Thus, of 1,402 thyrotoxic cases recently reported by Boothby (15), 366 developed thyroadenomata after periods averaging 16 years after appearance of the goiter. If we agree with Marine and Lenhart's well substantiated arguments on the compensatory nature of *all* thyroid hyperplasias, then we must accept that all toxic thyroadenomata develop in glands showing previously cellular proliferation due to toxic or other injury, therefore in a potential hypofunctional condition. This consideration is a strong argument against the conception of a primary idiopathic hyperfunction and for the dysthyroidism hypothesis in the genesis of Graves' disease.

The infectious origin of Graves' disease seems clear in a number of cases. The symptoms are known to appear as a sequela to acute thyroiditis following trauma or by extension from neighboring foci, also after typhoid fever, tuberculosis and other bacterial infections. They sometimes can be traced to remote focal infections. According to the experience of McCarrison (44), Lane (45), Bate (46), Ebstein (47), and others, including the present writer, chronic intestinal toxemia is probably an etiologic factor in another group of cases. It may be noted that these same etiologic factors are frequently demonstrable in simple and endemic goiter (McCarrison). It may, then, be reasonably argued that the subsequent pathologic changes with clinical symptoms of thyrotoxic or hypothyroid type would be explicable on a common basis.

PATHOLOGICAL EVIDENCE IN FAVOR OF THE DYSTHYROIDISM THEORY

The Nature of Thyroid Hyperplasia It is believed that the "hyperthyroidism theory" has long obscured a clear conception of thyroid pathology and clinical deductions made therefrom. As long as we continue to regard hypertrophy and hyperplasia of the thyroid as good and sufficient evidence of hypothetical "hyperfunction," it remains impossible to correlate and interpret the known facts logically. If, however, the evidence already presented is deemed sufficient to demonstrate the inadequacy of this long accepted view, we are in a position to make unbiased deductions from the data in our possession.

The general nature of hypertrophy and hyperplasia may first be considered. These processes occur (1) under physiological circumstances in a normal organ when increased function is called for (examples,—increase in size of muscles in athletes, uterine hypertrophy in pregnancy, cardiac hypertrophy in mountaineers, hyperplasia in bone marrow after hemorrhage, etc.), (2) under pathological conditions when through injury to an organ by infection or trauma its function becomes impaired (examples,—hypertrophy of lymph glands, cardiac hypertrophy due to muscular or valvular lesions), (3) as pure growth anomalies (myomata, adenomata, carcinomata, teratomata, etc.), never accompanied by true hyperfunction.

The thyroid gland is one of the most important endocrine organs which control general cellular nutrition and growth. In higher organisms it is the seat of some of the most active metabolism. It is peculiarly reactive to extrinsic stimuli,—nervous, chemical and toxic. Its chief function is the synthesis of thyroxin, the thyroid hormone, a complex organic compound containing about 66 per cent iodine. The careful experimental and clinical work of Kendall and Plummer has made it probable that there is an exact quantum of thyroxin necessary for the maintenance of the normal nutrition of the tissues and organs at any given time. Growth puts an added strain on thyroxin production, since the chief function of the thyroid is anabolic (Janney). All evidence goes to show that the thyroid is under very delicate sympathetic nervous control, in turn influenced by central and very probably by hormonal stimuli—adrenalin—(Cannon, Lennhart and Bowmann). Anatomically and physiologically, the thyroid activity is also stimulated by increased iodine content

of the blood, for which element, because of this gland's peculiar necessity for iodine, it exerts a selective affinity

To meet these varying requirements rapid physiologic and structural changes are obviously necessary. Among such, normal colloid formation may perhaps be included, this is possibly a means of storage of materials needed in thyroid metabolism. Hypertrophy and hyperplasia occupy a prominent place in such necessary changes. Thus the gland, due to additional requirements of the growing embryo, shows a normal increase in size during pregnancy. Conversely, during inanition it has been experimentally shown to decrease in size as well as to increase in size on meat ingestion (Bensley's opossum experiment). *It is very likely on account of the above causes that hyperplasia is frequently required in the case of the thyroid during the normal course of existence, even when no thyroid disease is present* [White et al (48)]

Marine and Lenhart (49), to whom we are indebted for important studies in this regard, may be quoted as follows

"In man the greater proportion of thyroids showing histological changes toward goiter formation are not associated with detectable clinical manifestations. Most of these milder degrees of thyroid changes spontaneously right themselves when the underlying or accompanying disease disappears, as, for example, the hyperplasia associated with influenza, or typhoid, or pregnancy, etc., rarely comes to clinical notice. Thus it is that all autopsy series show such a great proportion of thyroid changes without detectable clinical manifestations."

From these considerations, it is evident that hyperplasia in thyroid conditions develops on account of the same causes as in all other organs and tissues and is due to (1) increased physiological requirements (examples,—goiter of puberty, pregnancy, etc.), (2) decreased function because of trauma, infection and other pathological processes either in the thyroid or in the organism in general (examples,—acute thyroiditis with acinar hyperplasia, thyroid enlargement in acute and chronic infectious diseases, endemic goiter, hyperplasia after thyroidectomy) decreased function due to under-nutrition, including iodine starvation (examples,—goiters in poorly fed puppies, lambs and children)

The Relation of Iodine to Thyroid Structure has been thoroughly studied by Marine and Lenhart, who state

"Withholding iodine increases the extent of the hyperplasia following partial removal (Marine), and also causes hyperplasia without partial removal (Baumann)

"The administration of iodine causes active hyperplasia of all

animals to revert to the colloid state, prevents the occurrence of active hyperplasia following partial removal of glands which otherwise would undergo hyperplasia

"The administration of iodine prevents hyperplasia of the thyroids of puppies from bitches in which three-fourths of the gland has been removed

"Normal thyroids of all the animals examined have the highest and marked hyperplasias, the lowest iodine contents

"The administration of iodine-containing compounds to the animal in any form and by any method is rapidly followed by its storage in the thyroid in quantities that bear no relation to the iodine content of the other tissues

"The rapidity of accumulation and the amount of iodine thus taken up by the thyroid depend on its size and the degree of active hyperplasia

"The physiological activity, as determined by the nitrogen excretion (Roos), by the loss of body weight (Marine and Lenhart), and by the acetonitrile reaction (Hunt, Hunt and Seidell), depends principally on the amount of iodine in organic combination

"It has been shown (Marine and Williams, Marine and Lenhart) that in dog, sheep, pig, ox and human thyroids there is a quite constant minimum percentage of iodine necessary for the maintenance of normal gland structure

"While practically nothing is known of the causes leading to the iodine deficiency in the animal, the above facts, beyond doubt, show that the increased growth and divisional activity of the thyroid cells are intimately associated with a decrease in iodine, and that the increased iodine content is similarly associated with a decreased growth and divisional activity of the thyroid cells. On this basis one would expect to find thyroid changes resulting from any cause which diminished the intake or assimilation of, or increased the body demands for iodine, and that, therefore, all thyroid changes would be compensatory in nature and secondary to more fundamental causes, perhaps nutritional in nature"

The Histo-pathology of Thyrotoxicosis and its Relation to the Iodine Content follow the same laws as they do in morbid processes in general and in other thyroid conditions, normal and abnormal. This assertion is based upon the following observations

- 1 The histological changes of the thyroid gland in thyrotoxicosis are fundamentally the same as those occurring in other goiters. The differences are chiefly those of degree. The rapidity and succession of periods of hyperplasia and involution also play their part, also the age of the affected individual and the goiter. The hyperplasia of exophthalmic goiter varies with pregnancy or puberty, precisely as do simple goiters. Colloid goiters in thyrotoxic patients are not infrequent

- 2 The iodine content of the gland in thyrotoxicosis varies inversely with the degree of hyperplasia and in general is modified by the same influences as in other thyroid conditions. The hyperplasia in thyrotoxic goiters can be reduced by administer-

ing iodine just as is possible in the case of simple goiters. The thyrotoxic goiter is poor in iodine as is simple goiter. Degenerations, atrophy and sclerosis may follow the hyperplastic stage in thyrotoxicosis as in thyroid adenoma with development of myxedema or cretinism in either case (Marine and Lenhart, McCarrison)

3 There is a lack of parallelism between the degree of hyperplasia and the toxic clinical symptoms which would argue for a differing etiology of each and against a direct cause and effect relationship (see also histologic discussion under "hyperthyroidism theory")

The hyperplasia of thyrotoxicosis is best explained, just as in other thyroid hypertrophies, as an attempt at compensatory regeneration to make up for cellular exhaustion and injury due to toxic or other cause. We have thus an acceptable explanation for the thyroid hyperplasia of Graves' disease arising from local or focal infections, intestinal toxemia and bacterial infections,—hyperplasias not susceptible of reasonable explanation by the hyperthyroid theory. In order that the supply of thyroxin under these circumstances be maintained at the normal level, increase in the secretory tissue is necessary in order to compensate for exhaustion of the acinar cells through toxemia.

In thyrotoxic cases arising after nervous shock or exhaustion, the hyperplasia is again explicable on the same general basis. Owing to exaggerated or deficient neuro-trophic stimuli in such cases, an abnormal cellular metabolism is set up with ensuing decrease in the normal quatum of normally functioning parenchyma, which condition elicits the stimulus to rapid hyperplasia.

The pathological processes, then, are essentially the same in all thyroid diseases, aside from the malignant.

They represent themselves by three stages: (1) the hyperplastic, (2) the involuntary, recovery or colloid, (3) the exhaustion or premature atrophy or myxedematous stage (Marine and Lenhart, McCarrison). In exophthalmic goiter, the hyperplastic stage predominates and the morbid process is usually arrested at the first or, more rarely, at the second, or third. Not only may the lesions of thyrotoxic goiter be reasonably explained upon this basis, but also those of endemic goiter and hypothyroidism. In ordinary colloid goiters, the process ceases with the second stage,

whilst in hypothyroidism the atrophic processes predominate, not without, however, frequent secondary development of hyperplasia and colloid formation (goiters of cretins)

This pathological consideration would be incomplete without reference to the work of Wilson (12) and Plummer (13) on the pathological classification of surgical goiter. As is also clearly shown by Boothby's (15) recent presentation of these data, goiters of thyrotoxic patients may be classified into two main groups: (1) toxic adenomata, (2) exophthalmic goiter. The former group is distinguished by the development of discrete adenomatous nodules which only after an average period of 16 years are followed by toxic symptoms. The second type is distinguished by a diffuse parenchymatous hypertrophy followed within a few years, at most, by more severe clinical symptoms, including exophthalmos, thrills, and bruit. Great credit is due these Mayo Clinic workers for the thoroughness with which this differentiation has been worked out in a large number of cases. C. P. Howard (7) has, however, pointed out that a similar classification of thyrotoxic cases had already been present by Buschan (50) in his monograph published in 1894. Plummer, who has long adhered firmly to the hyperthyroidism theory, formerly ascribed both classes of these cases to hyperthyroidism, on the basis of the presence of hyperplasia. In his most recent article (14) he regarded, however, the toxic adenomata as due to "pure hyperthyroidism," but entertains the possibility of an altered thyroxin molecule in the exophthalmic goiter group.

The importance of this grouping from the pathological and clinical standpoint is undoubted. The acceptance, however, of a differing pathogenesis seems scarcely justified by the facts known at present. According to the broad conception of thyroid pathology established by Marine and Lenhart, as well as McCarrison, it is likely that the differing pathological and clinical manifestations are largely merely those of degree, inasmuch as hyperplasia and essentially the same clinical manifestations are present in both classes of cases. The thyroid, in the case of the toxic adenoma, may, through the slow influence of hereditary thyroid deficiency, under-nutrition, or chronic toxemia develop discrete hyperplastic nodules which may suffice to afford a complete compensation as to function (non-toxic thyroadenoma). Only after a prolonged continuance of the exciting factors, a

metabolic disturbance ensues with development of toxic symptoms of a mild type leading but rarely to the severer manifestations of Graves' disease (toxic thyroadenoma). On the other hand in the typical cases of exophthalmic goiter (Group II) the pathological excitant is stronger and the thyroid reaction is more universal (diffuse hyperplasia), but less effectual, since in a much shorter period thereafter and sometimes concurrently, the severe toxic symptoms (exophthalmic, bruit, thrills, greatly increased basal metabolism, etc.) set in. On a similar basis may be explained those peculiar cases of thyrotoxicosis which ensue within a few days after fright or other great emotional shock where the disturbance of metabolism begins before the compensatory hyperplasia has time to become manifest.

The chief difficulty in interpreting the pathological lesions of thyrotoxicosis has, it seems, lain in an over-zealousness to find pathological confirmation of the hyperfunctional hypothesis together with insufficient appreciation of the very considerable variety of factors involved. The frequency of hyperplasia, the low iodine content, and the tendency to late fibrosis in the thyrotoxic goiter would demand evidence of deficient thyroid function in the clinical and metabolic phenomena of the disease. That such evidence may be actually present will now be emphasized.

CLINICAL AND METABOLIC EVIDENCE FAVORING THE DYSTHYROIDISM THEORY

Toxic and Trophic Symptoms. Certain symptoms of thyrotoxicosis are so striking and demand so much attention through their annoying nature that they have always occupied the foreground of attention. The mental changes, the exophthalmos, the tachycardia and tremor may be mentioned. They represent toxic symptoms characteristic of the disease. It is, however, not generally recognized that there exist a considerable number of clinical manifestations which, though often of minor practical importance, yet demonstrate clearly the fundamental nutritional disturbance also present in the Graves' disease. For this reason, the present writer (40) classified some years ago the symptoms on this basis. They are set forth in the following table in more detail.

Classification of the Signs and Symptoms of Thyrotoxicosis
(Janney)

I Toxic Signs and Symptoms of Thyrotoxicosis

Nervous System

Psychic Irritability, restlessness, excitability, insomnia, psychoses

Sensory Hyperesthesia, pruritus, flashes of heat

Motor Tremor, twitchings, trembling, rarely convulsions

Special Senses Auditory and luminous phenomena, ocular pain

Autonomic Exophthalmos and special ocular signs Secretory Sudorrhoea, epiphora, salivation, increased intestinal secretion, etc Nausea, vomiting, diarrhoea through smooth muscle stimulation Erythema, purpura, dermatographia, urticaria, transitory oedema

Cardio-vascular Tachycardia, cardiac hypertrophy, palpitation, arterial pulsation, functional murmurs

Respiratory Tachypnoea, dyspnoea

Hematopoietic Toxicity of blood, lymphocytosis, mononucleosis, decreased bacterial alexines

Metabolism Loss of weight, increased metabolic rate, excessive breakdown of protein, increased excretion of protein metabolites Rise of temperature

Genito-urinary Toxicity of urine

II Trophic Signs and Symptoms, including those of Thyroid Deficiency and other Endocrine Deficiency

Thyroid Hypertrophy, hyperplasia, sclerosis in old cases

Cutaneous Atrophy, pigmentation, hair changes (premature greyness, brittleness, alopecia), nail changes (thinness, seaming, brittleness), myxedematous patches, scleroderma Dentition premature erosion and caries

Cardio-vascular Fatty and sclerotic lesions in myocardium and vessels, myocardial insufficiency, mitral insufficiency, cardiac hypertrophy

Organic Various degenerations in somatic organs, albuminuria

Muscular Weakness, atrophy, degeneration

Osseous Imperfect ossification, thinning and increased fragility of the bones, ununited fractures, rarely osteomalacia

Metabolic Delayed glucose assimilation, increase of nitrogenous retention through thyroid therapy, normal or subnormal

metabolic rate in dysthyroid cases

Ductless Glands Presence of symptoms and lesions of hypofunctional type referable to the pituitary (polyuria, polydipsia, fat distribution), thymus (hypertrophy), suprarenals (cutaneous pigmentation, asthenia, diarrhoea), pancreas (alimentary glycosuria, diabetes), lymphatic system (lymphatic hypertrophy, splenomegaly, enlarged tonsils and adenoids), gonads (hypoplasia, decreased libido, dysmenorrhoea, amenorrhoea, menorrhagia)

REMARKS UPON CLINICAL CLASSIFICATION OF SIGNS AND SYMPTOMS OF THYROTOXICOSIS

Many of the trophic changes are of apparent triviality. They are frequently overlooked by clinical observers, perhaps partly on account of the ease with which the diagnosis of thyrotoxicosis can usually be established, merely from the classical toxic symptoms. The cutaneous and blood changes are practically always present and are indeed diagnostic of thyrotoxicosis. The bony lesions are frequent in cases beginning in earlier life. They are not usually observed, as roentgenograms are not often made in these cases. The lesions in the organs are found only at post mortem. Thus Askanazy (51) notes in each case examined widespread fatty infiltration and fatty degeneration of the voluntary muscles. It might be argued on excellent grounds that such lesions are rather of toxic origin, but it will be remembered that similar changes are noted in cretinism and myxedema, so it is preferred to regard them as trophic rather than toxic.

Endocrine Interrelationships in Thyrotoxicosis As is well known, the condition of hypothyroidism quite often appears in association with hypopituitarism and, indeed, more complex pluriglandular syndromes. If, then, there be clinically observed in Graves' disease accompanying hypofunctional disturbances in other endocrine organs, such may be regarded as additional indirect evidence that a similar, i. e., hypofunctional process, prevails in the thyrotoxic thyroid gland. Such a state of subfunction may thus affect the nutrition of other ductless glands, leading to hypofunctional disturbances in these organs. On the other hand, it is possible that lesions in other ductless glands are due to thy-

roid toxemia or even, in the case of the suprarenals, causative of the thyroid condition (See below)

Occasionally, pituitary lesions are found at autopsy of persons dying of exophthalmic goiter. As emphasized by Hofstaetter (52) and Salmon (53), certain of the trophic symptoms of this disease (see table) may be of pituitary origin. Improvement noted at times on administration of the pituitary preparations would substantiate this view.

Simonds (54) and others have reported hyperplasia and atrophy in the suprarenals in thyrotoxic subjects. The pigmentation and asthenia may be possibly due to accompanying suprarenal involvement. We may, however, not be dealing with cause and effect so far as the possible influence of the thyroid state in Graves' disease on the suprarenal is concerned, for the reverse may be true and adrenal disturbance play a part in the thyroid condition, as suggested by Cannon's researches on the stimulatory effect of adrenalin on thyroid secretion. The recent experiments of Marine and Baumann (55) are of much interest and possible importance in this regard. These investigators found a rise in the basal metabolism to follow injury to the suprarenal cortex in rabbits, accompanied by certain cutaneous and nervous phenomena similar to such found in Graves' disease, but without production of the complete clinical picture. Adrenalin has likewise been shown by Tompkins, Sturgis and Wearn (56), Sandiford (57), and Marine and Lienhart (58) to cause a rise in the respiratory exchange. Removal of the suprarenals causes thyroid hypertrophy. From all this work, it is likely that the suprarenals exert an effect or control on normal, and possibly abnormal, thyroid metabolism. They may thus play a rôle in the etiology of exophthalmic goiter, the exact mechanism of which requires elucidation.

The association of diabetes mellitus and Graves' disease has been reported by various authors [v Noorden (59), Ewald (60), Falta (61), Sattler (10), 40 cases]. The frequent presence of alimentary glycosuria (many observers) and an increased blood glucose curve [Hamman and Hirschman (62), Geyelin (63), Janney and Isaacson (64)], would suggest a pancreatic affection in Graves' disease. On the other hand, the thyroid itself exerts an influence on carbohydrate metabolism as shown by the de-

velopment of hypoglycemia after thyroidectomy (Janney and Isaacson).

A diffuse adenohyperplasia is regularly found in Graves' disease (Kocher, F v Muller) This may include the tonsils, spleen, and intestinal follicles The lymphoid cell infiltration of the thyroid itself is best considered an expression of the same general process It is probable that the thymic enlargement, in spite of efforts to bring out a more specific relationship, is but an instance of the general *status thymolymphaticus* present [Capelle (65), see also Eddy's (66) recent review of the literature] The lymphocytosis and mononucleosis present in both hypothyroidism and exophthalmic goiter are probably due to this *status lymphaticus* It will be recollected that a similar hypertrophy of the lymphatic system, at times accompanied by thymic enlargement, takes place in hypothyroidism, Addison's and other endocrine diseases

Signs and Symptoms of Uncertain Etiology The emaciation and weakness of Graves' disease, though referred to the toxic and trophic group respectively, can be regarded as characteristic of either group Emaciation is not so uncommon in hypothyroidism Indeed, the musculature may show definite wasting, weakness can be caused by the toxemia, but again it is one of the earliest symptoms of hypothyroidism Emaciation and weakness may again be possibly relegated to accompanying supra-renal deficiency

The cardiac hypertrophy may be compensatory in early cases and due to the tachycardia It may thus be regarded as a sequela of the toxic stimulation On the other hand, in cases of goiter heart it may be due to myocardial degeneration which may be either toxic or trophic in origin

The diarrhoea may, as indicated in the table, be ascribed to toxic stimulation of the intestinal musculature It may, however, possibly be due to an accompanying supra-renal deficiency or to deficient pancreatic secretion (fatty diarrhoea of thyrotoxicosis).

Certain of the metabolic phenomena ascribed to accompanying endocrine disturbances are of somewhat uncertain etiology Thus the creatinuria may be due to toxic breakdown of muscle as well as to muscle disintegration due to lack of normal repair and replacement processes

CLINICAL DYSTHYROIDISM

Aside from the occurrence of the above mentioned thyroid deficiency signs and symptoms in typical cases of Graves' disease, there is a group of cases in which the symptoms of myxedema are frankly intermingled with those of Graves' disease. For this condition the term "dysthyroidism" is particularly applicable, although, for reasons advanced in the present paper, the same designation might well be applied as synonymous with thyrotoxicosis. Usage has, however, restricted the use of this term to cases showing a definite combination of myxedema and thyrotoxicosis.

It is significant that myxedema never precedes thyrotoxicosis, but often follows it. This behavior would be expected from the pathologic and metabolic data already emphasized. Hand-in-hand with the incipient hyperplastic changes are seen the increase in the metabolic rate, protein loss, rise of temperature, and the development of toxic manifestations. As the period of cellular exhaustion, atrophy and sclerosis gradually supervenes, the clinical picture of myxedema slowly develops. On the other hand, cases have been reported by Sollier (67), Jolly (68) and Osler (69) in which the thyrotoxic and myxedematous symptoms occurred simultaneously.

Every experienced internist has observed examples of clinical dysthyroidism which are much more common than usually appreciated, as emphasized by Bertine (70), who reported from the Cornell Medical Clinic in New York, among 133 thyroid cases, 33 cases presenting in no uncertain way a combination of thyrotoxic and hypothyroid symptoms. Thus a combination of tremor, sudorrhoea and at times exophthalmos and tachycardia may be present in patients showing the hypothyroid type of obesity, mental hebetude and asthenia. In surgical myxedema there may likewise be observed typical examples of interposed hypothyroid and thyrotoxic symptoms in which the thyroid remnant left at operation still remains toxic and, in addition, indeed, is functionally deficient through removal of the bulk of the gland. It may be here mentioned that nervousness and tremor are not necessarily always thyrotoxic in origin, as Horsley (71) has observed a nervous excitable stage in experimental athyroidism, and both Horsley (72) and McCarrison (44) have reported such symptoms in incipient myxedema. *The existence of clinical dys-*

thyroidism is a potent argument in favor of the acceptance of the dysfunctional theory The fact is apparent that both the toxic and trophic symptoms must be caused by morbid processes simultaneously occurring in the same thyroid gland, which lead to the discharge of secretion deficient in quantity but toxic in quality

THERAPEUTIC EVIDENCE

A real improvement on thyroid medication has been rarely reported in certain cases of Graves' disease and dysthyroidism, particularly those exhibiting marked myxedematous signs (Murray, Dock, *et al*) This observation has been substantiated by the metabolic studies of Janney (40), as well as Halverson, Bergem and Hawk (43), who noted an added retention, not a toxic loss, of nitrogen and other protein metabolites on thyroid administration in Graves' disease This reaction does not occur in control cases Such observations constitute a demonstration of the normal anabolic function of the thyroid gland in thyrotoxicosis and are of considerable importance as supporting the dysthyroidism theory

THE HORMONE HYPOTHESIS OF GRAVES' DISEASE

Adherents to the dysthyroidism theory have made various attempts to explain the exact nature of the toxic thyroid secretion Lampe, Liesegang and Klose (20) accept an altered molecular constitution of the thyroid hormone In 1918 Janney (40) emphasized that the "hormone hypothesis" supplied a plausible explanation for the complex manifestations of the disease This view may be quoted in abstract in its original form

"All evidence tends to indicate that the thyroid hormone is a synthetic product It is certainly built up by the thyroid from inorganic iodine and other substances possibly related to the indol-containing amino-acid, tryptophane It is possible that one or more of these intermediate substances is toxic, and, indeed, identical with the products arising in the breakdown of the hormone in the body It is likewise possible that various factors might disturb the normal synthesis of the hormone, the result being the premature discharge of the toxic intermediary product into the circulation The factors producing this condition might be disturbances in the nervous control of the thyroid metabolism, such as could be produced by fright, emotion, shock or direct organic injury such as trauma, thyroiditis, or again, histologic and gross changes in the parenchyma of the gland, that is, the well known causes of exophthalmic goiter

"The result of the premature discharge of the hypothetical toxic intermediary product would be an impoverishment of the gland of the thyroid hormone, which would explain the fact that Graves' disease goiters are poor in iodine, and especially in the active alpha-iodine pro-

teins The decreased production of the normal hormone due to the cause mentioned would tend to be accompanied or followed by the signs of thyroid insufficiency Thus the deficiency symptoms (Group 2) can be accounted for, also the concomitant occurrence of hypothyroid and hyperthyroid symptoms, and the tendency of exophthalmic goiter patients to develop myxedema

"The frequent failure of the pathologic picture to coincide with the clinical (see the foregoing) can best be explained by these views, which do not strictly necessitate histologic change at the beginning, but rather a defective endocrine secretory metabolism as the ultimate cause of exophthalmic goiter

"According to our hypothesis there is present in the thyroid and blood of exophthalmic goiter patients a toxic substance This view is substantiated by the experiments of Caro, confirmed by Klose, by demonstrating the toxicity of the urine from exophthalmic goiter patients, also recently by Blackford and Sanford, who found a depressor substance in the thyroid and serums of such patients"

R G Hoskins (73) and C P Howard (7), among others, have favorably regarded such an hypothesis Plummer (38) followed by Boothby (38), incline recently to the same viewpoint, the latter erroneously ascribing it to Kendall

However desirable it is to discard the time-worn "hyperthyroidism" for the "dysthyroidism theory" it seems timely to remark that the "hormone hypothesis" is lacking in proof which must include the isolation and identification of a thyrotoxin, chemically related to thyroxin In the present meager state of our knowledge, this hypothesis is merely deserving of recognition as a working idea for the stimulation of further studies in the difficult field of thyroid research

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THE POSITIVE ACHIEVEMENTS OF ENDOCRINOLOGY

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The recent appearance of a number of hypercritical articles on endocrinology tends to create a state of unwarranted skepticism toward this branch of medicine. So much stress has been laid upon the negative accomplishments that it is not amiss to present a brief review of its positive achievements.

From the standpoint of the clinician all investigations center toward one object—progress in diagnosis and in therapy.

While attending a large medical meeting recently, the writer was impressed by the negative tone that dominated most of the papers submitted. So much was said of what had *not* been accomplished and so little stress was laid upon what *could* be accomplished in therapy, that most of the physicians took back with them a mass of unknowns with which to combat their perplexing daily problems.

It is distinctly desirable to maintain a critical attitude toward anything new in medicine, and such an attitude is an excellent balance to the unwarranted claims of many misguided enthusiasts. However, there has been so much progress made in many branches of medicine within recent years that it is of prime importance to call the positive achievements to the attention of the medical profession, and to place the new facts in the hands of the general practitioners to strengthen their armamentarium in the diagnosis and treatment of disease.

The interested practitioner who studies endocrine literature is bewildered by the combat between the enthusiasts and the conservatives. It is most unfortunate that so many extravagant claims for endocrine therapy have been made by certain mercenary manufacturers of organic products. To them most of medicine is endocrinology and they supply the physician with ready-made formulae for the cure of every disease or condition that flesh or mind is heir to. Furthermore, the suggestiveness of the positive facts and the large number of unknowns in endo-

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crinology stimulate the imagination. This has led to literary outbursts of enthusiasm which present certain suggestions and probabilities as established facts.

For the past five or six years, the writer has conducted a clinic for the systematic study of medical problems from an endocrine standpoint, making as careful clinical and laboratory observations along these lines as facilities permit. This work has demonstrated that this branch of medicine, in spite of its shortcomings, has made positive contributions to clinical medicine.

In order to judge of the progress of any branch of medicine we must take into account the age of the subject and compare its achievements with those of other branches of medicine. Endocrinology dates as such only from 1889, but in this brief period it has made progress proportionately greater than any other branch of medicine.

Although conversant with the experimental and laboratory literature, being primarily a clinician, I shall confine myself principally to the contributions made to clinical medicine, to therapy, and to public health medicine.

We may divide the progress in endocrinology into several categories: (1) progress in the well-established syndromes of the various ductless glands, (2) contributions of endocrinology toward various non-specific branches of medicine, (3) contributions to therapy, and (4) contributions to public health. In the definite syndromes I shall discuss only the generally recognized ductless glands.

DEFINITE CLINICAL SYNDROMES

The thyroid syndromes were to some extent appreciated in 1850, when Curling first described cretinism. This was followed, in 1873, by the description of myxedema, by Sir William Gull. In 1882, Reverdin showed that the complete removal of the thyroid produced myxedema—while in 1888, only thirty-four years ago, Sir Felix Semon grouped all the various facts about the thyroid and proved conclusively that cretinism, myxedema and post-operative myxedema are due to the same cause—thyroid deficiency. In 1891, Murray, a pupil of Sir Victor Horsley, presented the first case of myxedema treated successfully by oral administration of thyroid extract. The effect of this communication was far reaching because it not only established a cura-

tive therapy for myxedema, but it established the therapeutic principle that, given a deficiency of a certain endocrine gland the oral administration of a dried extract of that organ can be curative

The description by Graves in 1835, by Parry, 1786-1815, by Flajani, 1802, and by Basedow in 1840, of the syndrome of exophthalmic goiter was followed by the work of Kocher, who demonstrated that partial thyroidectomy could cure exophthalmic goiter. And thus was established the surgical treatment of exophthalmic goiter, which later came to include the use of thyroid vessel ligation, either complete or preliminary, by the Mayo Brothers, and the perfection in technique in the surgery of the thyroid, by Crile. The contrasting syndromes of myxedema and cretinism, and exophthalmic goiter, led to the conception of two disturbances of function in the ductless glands—hyper-activity and hypo-activity, one being regarded by many as evidence of over-activity and the other evidence of under-activity.

In 1915, Hertoghe (and later Levi and Rothschild) described clinical conditions in which thyroid deficiency occurred in a very mild form—the so-called *forme fruste*. *Forme fruste* types of over-activity of the thyroid have also been described, but since many of the symptoms of this type of disturbance occur in various neurotic conditions, it was largely a matter of judgment as to whether, in the absence—or even in the presence—of an enlargement of the thyroid gland, the physician was dealing with a condition of neurasthenia or of hyperthyroidism.

Boothby, Aub and others, a few years ago, however, established the fact that an increase in the basal metabolic rate, in the absence of fever, is nearly always an indication of hyperthyroidism and that the degree of apparent hyperthyroidism is in proportion to the increase in the basal metabolic rate. This important fact, while generally accepted in clinical medicine, is of comparatively very recent date.

Still more recent is the isolation of thyroxin, a definite hormone, by Kendall of the Mayo Clinic, and the demonstration of its effect on metabolism.

The etiology of hyperthyroidism, however, is still in doubt. The question as to whether nervous influences initiate the condition, or whether the hyperthyroidism is behind the nervous element has not yet been settled. There is some evidence, also, that

other ductless glands may play an important rôle, either primary or contributory, and that infections and diet are important factors. The differential diagnosis of hyperthyroidism from states of autonomic imbalance and the relation of hyperthyroidism to basal metabolism have been much discussed. This discussion seems due largely to the geographical location of the cases, the frequency of endemic goiter in iodine-poor districts, and the greater frequency of autonomic imbalance in urban districts.

In the etiology of thyroid deficiency more progress has been made. The work of McCarrison in producing goiter in animals by administering fecal matter threw some light on the subject. Subsequently, Marine made the clinically important observation that the absence of iodine in the food or drinking water is a specific factor in the causation of endemic goiter. Furthermore, he and others proved that by increasing the iodine content of the food or the water endemic goiter could be made to disappear.

Pituitary Syndromes Pituitary syndromes were first recognized in 1887, when Minkowski described acromegaly. In 1889, more extensive contributions by Pierre Marie established this syndrome, while, in 1886, Sir Victor Horsley cited experimental evidence that the pituitary is necessary to life, though this statement has been controverted by Aschner. In 1908, Paulesco, of Bokhara, removed the pituitary gland, while in 1911, Cushing, in his memorable monograph, reported evidence that the adipo-genital syndrome of Froehlich is due to a pituitary deficiency. This was followed by the cure of diabetes insipidus by injections of pituitrin. Furthermore, it is evident, on clinical examination, that in diabetes insipidus the patients show evidence of pituitary disease. Lately, a report has been made, by Blumgart, that the same results could be obtained in diabetes insipidus by spraying the pharynx with pituitrin as by hypodermic injections. Although in recent years the glandular origin of diabetes insipidus and of the Froehlich syndrome has been questioned by Bailey and Bremer, Camus and Roussay, and others, the suggested origin being a lesion in the tuber cinereum, the efficacy of pituitrin, however, has not been questioned. There have also been some encouraging reports of the results of treating diabetes insipidus by dried extracts. It must be remembered that all these are facts of very recent origin.

The work of Cushing has taught us to recognize pituitary

tumors It has further taught the various manifestations of pituitary disease It has called attention to syndromes similar to those of a pituitary tumor without the eye symptoms, such as pituitary headache and the various forms of pituitary syndromes, it has suggested a possible endocrine (pituitary) origin for epilepsy Furthermore, the study of typical pituitary syndromes indicates the frequency with which this condition occurs Englebach has supplied a masterly classification of pituitary diseases which has helped to clarify the various syndromes

The therapy of pituitary syndromes, while it has as yet distinct limitations, has demonstrated definite results These conditions have been accurately described only within the past ten years and the recognition of the syndromes have resulted in operative procedures on pituitary tumors, with notable results or the relief of the conditions by x-ray therapy Progress in other forms of treatment of pituitary syndromes has been made, such as the use of pituitary extract in alleviating the so-called pituitary headaches and the abdominal crises We have, however, been unable to influence by therapy such conditions as acromegaly Although reports of reduction in weight, and acceleration of genital development, in pituitary syndromes have been made, these are still questionable for, in many of the instances, the genital development is merely a retarded puberty and, in my experience, weight reduction by pituitary extracts is still an unsolved problem

Disturbances of the Adrenals Disturbances of the adrenal glands were really recognized by Addison in 1855 Since then various minor grades of Addison's disease have been described Since injury to the adrenals—as by hemorrhage or infections—produces symptoms similar to those of a mild Addison's disease, it is believed, on clinical grounds, that a condition of adrenal insufficiency occurs in various infections and in neuasthenia This statement has been questioned by experimental physiologists because of their inability to reproduce the condition in animals The work of Cannon on the discharge of adrenalin in emotional and psychical states has been of tremendous importance in establishing a definite physiologic status for the adrenals, although it has not been, as yet, of very great clinical value The recognition and description of adrenal tumors, as well as the description

by the French of the condition known as "virilism," is a definite contribution to clinical medicine

The adrenal cortex has been shown to be extremely important in physiologic processes, indeed, it is pretty definitely established that the adrenal cortex is essential to life. The recent work of Marine and Baumann indicates the importance of the adrenal cortex in heat production and respiratory exchange and suggests its rôle in hyperthyroidism, though the work still needs corroboration.

The Thymus Gland With regard to the thymus gland the progress has been comparatively slow. It is definitely established that the thymus persists throughout childhood and disappears in adolescence. It is enlarged in hyperthyroidism. It is enlarged in cases of status lymphaticus. It produces certain respiratory symptoms in childhood. It is enlarged in certain forms of acute lymphatic leukemia. Certain tumors may arise from it. However, clinical study of cases with persistent thymus shows that thymic patients frequently develop pituitary syndromes and mild grades of the so-called Addison's syndrome. Such patients very often have small hearts and small blood vessels. Timme has studied the compensatory mechanism seen with the persistent thymus.

The Pineal Gland Quite recently, attention was called to the disturbances of the pineal by Frankl Hochwart, in his description of a case of precocious development of the genitals. In 1907 Bailey and Jelliffe collected about twenty-seven cases of this syndrome. This has taught us to recognize this lesion by the presence of an ophthalmoplegia interna, and precocious puberty. The precocious mental development of Frankl Hochwart's case has led to much speculation about the rôle of the pineal in mental deficiency, but the reports of therapy along these lines must still be considered critically.

The Gonads That the gonads have an internal secretion was proved definitely by Berthold, in 1849, by showing that the secondary sexual characteristics of cocks disappeared when the testes were removed, but not when the external duct or the nerves of those organs were interfered with. The artificial production of eunuchoidism, a procedure carried out from time immemorial, also demonstrates that the genital organs are responsible for the secondary sex characteristics. The work of Tandler

and Grosz on eunuchoidism indicated the important rôle in growth and development and in psychical manifestations of the genital organs. Lydston showed, years ago, that he could transplant testes successfully. Recently Steinach has been able to produce masculine characteristics in female guinea pigs by removal of the ovaries followed by transplantation of testes, and female characteristics in male guinea pigs by removal of the testes followed by transplantation of ovaries. Furthermore, he was able to produce hypertrophy of the interstitial tissue of the testes by ligation of the ducts, thus establishing an important method in endocrine experimentation.

The Ovaries With the advent of aseptic surgery and the frequent removal of diseased ovaries a great deal was learned about the physiology of these organs. While it is comparatively easy to recognize syndromes of ovarian deficiency by the absence of secondary feminine characteristics and by menstrual disturbances, it has not been so easy to recognize specifically syndromes of excessive activity of these glands. The importance of the corpus luteum in menstruation has been established. And there is a good deal of evidence which indicates that other ductless glands participate in ovarian function.

The Pancreas The fact that the pancreas has an internal secretion, probably originating in the islands of Langerhans, requires no proof at the present time. All our clinical and experimental knowledge of diabetes mellitus belongs to endocrinology. The recent work at the University of Toronto, where a substance, "insulin," which is capable of reducing hyperglycemia, has been prepared from the islands of Langerhans, seems to mark an important step in advance. Recently, also, the fact that Friedman was able to reduce hyperglycemia without producing myxedema after partial pancreatectomy by ligation and partial removal of the thyroid, suggests that in sugar metabolism, ductless glands other than the pancreas play an important rôle. Both of these facts are exceedingly important.

The Parathyroids Parathyreoprivic tetany is well known. McCallum showed that the injections of calcium salts would relieve tetany. Parathyroid administration for tetany has often been tried, but with questionable results. The recent work at Carlson's laboratory indicates that parathyroid removal produces tetany only in the presence of protein putrefaction, in the

intestine This seems to indicate, at least for the parathyroid, that it functionates not by producing hormones, but by detoxication

Glandular Interrelationships There is considerable evidence of glandular interrelationship, both from the clinical and laboratory sides, although laboratory experiments have until recently been unable to prove such relationship conclusively We have evidence of a pituitary and thyroid relationship, of a thyroid and adrenal relationship, of an adrenal and a pancreatic relationship, of a thyroid and parathyroid relationship, of adrenal and gonad relationship, and a gonad and thyroid relationship and a gonad and pituitary relationship Experimentally, however, Marine has recently shown that freezing the adrenal cortex increased the basal metabolic rate and hence perhaps affects the thyroid His later work has shown an adrenal cortex and gonadal relationship The explanation of these relationships on the basis of metabolic changes is untenable nor does it vitiate its endocrine mechanism Friedman's work on a thyroid-pancreas relationship has been previously mentioned The literature contains a vast mass of scattered data on such relationships

ENDOCRINOLOGY IN MEDICINE

The greater importance of endocrinology lies not so much in the recognition of the various specific syndromes as in its contributions to other branches of general medicine There is hardly a phase of medicine in which endocrinology does not play a rôle The profound lethargy and the lack of initiative of the Addison syndrome, the hyperexcitability of the hyperthyroid syndrome, the sluggish mentality of the myxedematous individual, the hyperexcitability and abnormal fears in exophthalmic goiter, the lack of initiative and psychical monotony of the eunuchoid, all indicate the important rôle of the ductless glands on the nervous system The increased metabolic rate of hyperthyroidism and its diminution in myxedema and in cretinism, the obesity of the pituitary syndrome and of the menopause, all demonstrate the profound influence of the ductless glands on metabolism Apart from the definite syndromes we may recognize endocrine manifestations in clinical medicine, principally as disturbances of development and disturbances of physiology

The appreciation of disturbances in development is com-

paratively new, and a great deal still remains to be accomplished, but there are certain positive data that have been contributed by endocrinology

1 We can recognize real cretinism and juvenile myxedema as causative factors in disturbances of growth and development in children

2 We have evidence of pituitary syndromes as causes of disturbance in development, such as the Froehlich syndrome and the Lorrain-Levi syndrome with its adiposity, its changes in bony growth and its delayed puberty, or partial or complete genital atrophy, and its increased sugar tolerance accompanied frequently by diabetes insipidus

3 In older children, we have evidence of disturbances as the result of genital deficiencies. The close relationship in bony growth between the pituitary and the gonads is an important factor in the recognition of disturbances of growth

4 We have evidences of retardation in mental development in association with thyroid deficiency, and in association with gonadal deficiencies

5 In a number of disturbances of mental development as in various forms of idiocy, there is clinical evidence of pluriglandular disease. But the specific glandular disturbances in these cases have not been worked out. There are encouraging reports in the literature of the treatment of these cases by organotherapy, but the results are as yet by no means uniform

ENDOCRINE ORGANS AND THE TEETH

A good deal of importance has been placed on the character of the teeth as evidence of endocrine disturbance. We may note large upper front incisors, increased spacing, overcrowding of the teeth, absence of, or rudimentary, upper lateral incisors, as evidence of gonadal deficiency, large or rudimentary canines as evidence of an adrenal disturbance, early decay of the teeth

The increased spacing is the most definite characteristic and simply indicates enlargement of the cranial bones and associated large pituitary. Overcrowding apparently suggests the reverse. The deficiency of the upper laterals, the significance of which is still undecided, seems to indicate certain gonadal developmental disturbances. These observations need statistical corroboration. There may be a basis for these conditions of the teeth. There is

apparently a regularity in the order in which the teeth appear and abnormalities of development of the teeth may indicate a retardation or disturbance at a specific stage of development. The subject offers a fruitful field for systematic investigation.

DISTURBANCES IN PHYSIOLOGY

Until very recently the major part of the medical student's course has been devoted to the clinical recognition of pathology, and the patient unfortunate enough not to have a recognizable lesion was usually regarded as unworthy of the serious attention by the average medical man. It is inconceivable that functional change should be manifest without structural change, but it is possible to have functional changes without appreciable structural change. While we are awaiting the recognition of the pathology of many diseases we must content ourselves with the recognition of abnormal physiology. Since the incertions are important factors in modifying function and perhaps in controlling function, the appreciation of the rôle of the ductless glands in any disease is of importance in those diseases where our present methods do not recognize a pathological basis. Thus, as a working hypothesis, we may say that the thyroid regulates the speed of metabolism, and possibly of function, the adrenals possibly modify the vigor of function, and the gonads may give character to function. But aside from these rather philosophical conceptions, endocrinology has contributed a great deal to the recognition and the treatment of functional disease.

From the group of the unknown so-called functional diseases, endocrinology has taught us to recognize certain distinct syndromes

- 1 The recognition of myxedema by a low basal metabolic rate as a cause for joint pains, for gastric symptoms, for drowsiness, etc

- 2 The recognition of mild grades of hyperthyroidism, with visceral or abdominal crises, with nervous symptoms, by means of basal metabolism determinations. The recognition of cardiac-neuroses, as evidence of hyperthyroidism, recognized by the application of basal metabolism studies

- 3 The recognition of functional pituitary syndromes which has followed the recognition of pituitary tumors. The characteristic pituitary headache, with abdominal cramps, visceral

crises, gastric and uterine crises, dysmenorrhoea, migraine, and, possibly, epileptiform attacks

4 The appreciation that gastric neuroses have apparently a constitutional basis, the appreciation that the increase in or diminution of the acidity is not a clinical entity, but a constitutional dyscrasia, the fact that such crises occur in hyperthyroidism indicates that the thyroid and the adrenals may play a rôle in these conditions, it is possible that an ulcer may be a terminal state of this condition. The frequent occurrence of duodenal ulcers after severe burns, and the demonstration of hemorrhages into the adrenals in these conditions as well as the work of Rogers on the effect of thyroid and suprarenal nucleoproteins on the nerve terminals of the stomach strongly suggests an endocrine factor

These are some of the contributions that endocrinology is making toward progress in clearing up very common apparently functional conditions

A few years ago, Eppinger and Hess called attention to constitutional states characterized by disturbance in the balance of innervation between the parasympathetic and the sympathetic branches of the autonomic nervous system, which they have grouped as states of "vagotonia" and "sympathicotonia." The frequent occurrence of these states in various syndromes of the ductless glands, particularly in hyperthyroidism, suggests a relationship of these conditions to the latter syndrome. Practically, however, it is very rare to find a pure state of vagotonia or of sympathicotonia. These constitutional syndromes do exist, but not in the well-defined groups as described by Eppinger and Hess, they are characterized by extreme variability, vagotonia existing at one time and sympathicotonia at another, or both existing together. The patients very frequently have many of the symptoms of what are ordinarily called mild grades of hyperthyroidism. The differentiation, however, can be made by a basal metabolic determination, whether hyperthyroidism is the result of autonomic imbalance or whether the reverse is true is still an open question. Rogers has been able to produce the gastric symptoms of autonomic imbalance by the injection of thyroid and suprarenal nucleoproteins. Other experimenters have obtained negative results, but the question must still remain open

Endocrinology has made a contribution to the clinical knowledge of obesity, for, on the basis of definite endocrinopathies it is possible to recognize different types of obesity, such as the generalized, the epigastric, the lower abdominal, the trochanteric obesity, and obesity confined to the lower extremities

Endocrinology has also fostered an important branch of medicine which we may term constitutional medicine or medical anthropology. The individual differences of people, their physiological and anatomical variations and their singular reactions to disease have been claimed to be due to the domination of certain ductless glands in their growth and development. This is a fruitful field for investigation and much stress has been laid upon this work by Sir Arthur Keith. At any rate the recognition of the pituitary syndrome of Froehlich, the Lorrain-Levi syndrome, as well as the description of the characteristics of the eunuchoid, by Tandler and Gross, has demonstrated that numerous individuals exist who apparently suffer little but who show the anatomic makeup of the Froehlich syndrome, the acromegalic, and the eunuchoid. The accurate descriptions of the various manifestations that result in such people has indicated that they may suffer from various functional disturbances on the basis of their singular makeup. Individuals with persistent thymus have also been described, with singular secondary characteristics as the result of their compensations. This is a branch of medicine which is still in its infancy, but it is a contribution of endocrinology which promises progress in certain functional diseases and especially in gynecology. Whether it holds realities or not only time and accurate studies will tell. It may help to solve individual reactions in disease.

ENDOCRINE FACTORS IN NEUROLOGY

The psychical changes and the changes in the physiology of the nervous system, such as the abnormal fears and excitability of hyperthyroidism, the sluggish mentality in myxedema, the lack of psychical initiative in eunuchoidism, the psychical manifestations of the over-sexed and the under-sexed, the psychical manifestations during menstruation, pregnancy, and at the menopause, etc., the relationship between the ductless glands and states of autonomic imbalance, all indicate the close relationship

between the ductless glands and the nervous system. It is also apparent that there are distinct psychical sex differences in the psychological manifestations of individuals and, although such conditions are apparent in every day life, they are not subject to laboratory proof, nor are they even subject at the present time to accurate psychological measurement. There are no psychological tests to differentiate a male from a female nor are there any reliable tests to measure the emotional states of individuals. These are all problems begging for solution.

Practically, however, certain pathologic changes have recently been described in the testes in cases of dementia praecox. There is also an apparently basic endocrine cause in the psychoses of pregnancy and post-partum states.

The occurrence of symptoms resembling Addison's syndrome has suggested that the adrenals are a factor in neurasthenia, but this has not been corroborated by laboratory proof. At any rate, it has proved a basis for organotherapy.

Homosexual tendencies and sex abnormalities suggest a ductless gland basis.

The Freudians are beginning to appreciate that the constitution of the patient is important in the psychology of the subconscious.

ENDOCRINE FACTORS IN GYNECOLOGY

The appreciation of the known facts in endocrinology is of prime importance to the gynecologist. Gynecological physiology largely constitutes the physiology of the ovaries, as well as the other ductless glands. Menstruation, ovulation, pregnancy and the menopause are due to definite physiologic processes of the ovaries, in which other ductless glands partake, hence it is essential for the gynecologist to be thoroughly familiar with endocrinology. The physiology of menstruation is not definitely known, but we do know that it is dependent upon the physiology of the ovary, probably the corpus luteum. The corpus luteum prepares the uterine endometrium for pregnancy, but when no pregnancy takes place the endometrium degenerates and menstruation occurs. Many gynecologists deny the participation of other ductless glands in the physiology of menstruation or in the physiology of the ovaries, but there is abundant evidence to the contrary. For example, the occurrence of amenorrhoea in a pituitary tumor and in the Froehlich syndrome, the occurrence

of amenorrhoea in hypothyroidism, the presence of dysmenorrhoea in pituitary disease, the occurrence of headaches similar to those present in pituitary tumors, at the menstrual period, the occurrence of hyperthyroid symptoms and the basal metabolic changes which have been described, at menstruation, all indicate a participation of other ductless glands in the physiology of the ovary. The ductless glands play an important rôle in the physiology of pregnancy, as is indicated by frequent enlargement of the thyroid, disturbances in metabolism, and obesity. Difficulties in labor also arise from abnormalities in development resulting from preadolescent disturbances of the ductless glands, such as the masculine type of pelvis and the infantile uterus, of the Froehlich syndrome. Gynecology has until recently been dominated largely by mechanical conceptions and the mechanical conditions of the uterus and ovaries on examination or found at operation are utilized to explain symptoms such as sterility and functional menstrual disturbances. Patients are curetted for these conditions without any benefit, when an infantile uterus (part of a constitutional Froehlich syndrome) is the cause. It is essential, therefore, for the gynecologist to recognize endocrinopathies in conjunction with his work, for sterility may be due to hypothyroidism, to an infantile uterus—part of the genital atrophy of the Froehlich syndrome, amenorrhoea may be part of the Froehlich syndrome or part of hypothyroidism, or of a primary genital atrophy which can be recognized by its secondary skeletal changes. The obstetrician must recognize that a masculine type of pelvis, occurring in pituitary syndromes, the result of a pituitary deficiency, may produce obstruction in labor and that the Froehlich type of patient may suffer from uterine inertia during labor.

The differentiation of the type of patient, so far as we know it at present—the eunuchoid, the pituitary and the thymic types with their secondary thyroid manifestations—is important in explaining functional menstrual disturbances. The menstrual disturbances in adolescence or in endemic goiter is another contribution endocrinology has made to gynecology. The menstrual disturbances occurring in autonomic imbalance are also important in the appreciation of functional gynecological disturbances.

Although these conditions are apparent, it is merely the

beginning of the positive contributions that endocrinology promises to gynecology. This does not necessarily mean that gynecology is now simplified and that all symptoms will respond at once to organotherapy, but it is a great step forward to the real biochemical appreciation of gynecological physiology. It is an advance from the mechanical conception, where a tilted uterus is made to account for sterility or for all symptoms. The appreciation of the constitutional factors in gynecology suggest organotherapy, but its value in gynecological disturbances must be determined entirely on its merits.

THE CONTRIBUTIONS OF ENDOCRINOLOGY TO PUBLIC HEALTH AND EUGENICS

In the short time that acute interest has been aroused in this branch of medicine, a few definite contributions have been made in the field of endocrinology to public health medicine. Marine demonstrated that endemic goiter is due to an iodine deficiency and he established a means for its prevention by placing iodine in the water supply, and the administration of iodides in various forms by mouth in goitrous districts. Iodine table salt is now commonly used in the middle west, as suggested by Hirschfelder, and in Switzerland iodized chocolate, for the prevention of endemic goiter.

It has not been generally appreciated that the recognition of the Froehlich syndrome and congenital eunuchoidism are often accompanied by permanent sterility and that the subjects should be advised against marriage. There are no greater marital tragedies than those of the over-sexed married to the eunuchoid or to the pituitary type with genital atrophy. But before advising such individuals one must be sure that the sterility is permanent. Occasionally the genital deficiency may improve after a normal sexual life incident to marriage.

TREATMENT OF ENDOCRINOPATHIES

We may divide the progress made in the treatment of endocrinopathies into surgical and medical therapy. Surgical therapy has given good results in thyroid disturbances, partial thyroidectomy for goiters and partial thyroidectomy or ligation of the superior thyroids for hyperthyroidism. The removal of pituitary tumors in the hands of such men as Cushing and Frazier, who have developed the most perfect technique, gives brilliant

results, and the medical profession is greatly indebted to them for their efforts to teach the recognition of these conditions. The discussion of surgical therapy on the testes and ovaries requires no comment. Recently there have been reports of successful results from testicular transplantation at the hands of Lydston and others, but the results are still questionable. The Steinach operation has been claimed to be successful as a means of stimulating the interstitial tissue of the testes for premature senility, but the results must still be considered critically. There has also been reported successful results following removal of one of the adrenals in epilepsy, but the results are still variable.

ENDOCRINE ORGANS AND X-RAY THERAPY

The x-ray and radium are powerful means of treating disturbances of the ductless glands. Practically the best results have been reported in the reduction of a large thymus, and in exophthalmic goiter. X-ray and radium applications to the pituitary, following operations, have also been more or less successful.

ORGANOTHERAPY

The establishment of the syndromes of hypo- and hyperactivity has led to the establishment of the hormone theory of ductless gland physiology. While it is apparently true that in many instances the discharge of a substance into the blood stream is the *modus operandi* of some ductless glands, this may not be true of all. Some of the ductless glands may act by detoxication, or by means as yet unknown. However, the hormone theory has established a basis for organotherapy. No matter what other explanations for organotherapy may be offered they are as yet largely theoretical and at the present time, when this form of therapy is efficient, it is substitution therapy, that is, if there is a deficiency of substances in the body that are normally supplied by a ductless gland that is diseased, this deficiency may be overcome by administering an extract of a corresponding normal gland. This has been definitely established in the case of myxedema when definite objective results are obtained by thyroid therapy. The fact that such specific results could be obtained led to the rational assumption which may or may not be true, that, given a deficiency of other ductless glands, similar results could be obtained. The proof of this assumption,

however, can only be established by actual trial in a sufficiently large number of cases under properly controlled conditions. Although the extracts of other glands have been used extensively it is most unfortunate that there is no satisfactory statistical study of any of them. However, certain definite results have been obtained with organotherapy, although there are also a large number of failures. The explanation of these failures may be that the underlying basis for such therapy does not apply to all glands, or that some products as they can be prepared today are not efficient. Progress along these lines can be made by establishing a new underlying basis or by the preparation of products that will be more efficient. We can summarize, however, the actual accomplishments in organotherapy at the present time.

- 1 Thyroid extract is a specific remedy for thyroid deficiency. Thyroxin, given intravenously, is a much more potent and more definite substance.

- 2 Pituitary therapy is indicated in states of pituitary deficiency, such as the Froehlich type or the Lorrain-Levi type. Practically, we have dried extracts of pituitary, anterior lobe and whole lobe, and pituitrin, the extract of the posterior lobe. Pituitary extracts have a limited value in pituitary syndromes. It is impossible to modify the physical manifestations of the pituitary syndromes by the use of pituitary extracts, it is questionable whether we can modify the obesity of the Froehlich syndrome in spite of the fact that reports of such results occur in the literature. It is also, probably, impossible to modify the genital deficiencies of the Froehlich or other pituitary syndromes. There are reports of success in this regard in the literature, but these are largely in adolescent children where spontaneous improvement in genital development occurs, since the genital deficiency in the successful cases was merely a retarded puberty. However, definite results can be obtained by the use of pituitary extracts for the relief of the characteristic pituitary headaches, and in some instances relief of the associated symptoms, such as the abdominal visceral crises, and the amenorrhoea and dysmenorrhoea which are the other manifestations of pituitary disturbances. We should not minimize the importance of these results for the patients afflicted with pituitary disease other than tumor suffer largely from these symptoms apart from the

adiposity and the genital disturbances. The adiposity often responds to dietetic therapy, whereas the genital deficiency may be temporary, slight or permanent, and in the latter instance is not as a rule amenable to therapy. Good results have also been reported in epilepsy, but with the well-known variations in the frequency of the attacks, and the response of epilepsy for a time to other forms of therapy, it would be best to hold these results in abeyance until statistical data with proper controls can definitely establish them.

Pituitary therapy is occasionally useful in modifying the menstrual disturbances incident to pituitary deficiency, such as amenorrhoea.

The dosage of pituitary extract is variable. Since we are attempting to supply an apparent deficiency of some substance in the body and since we have no way of measuring this deficiency quantitatively, we do not know the dosage. Practically, there is a marked variation in the quantities necessary to produce the effects that are possible to obtain, some patients requiring very small doses and others requiring enormous doses. Furthermore, there is a sex difference in the effect of pituitary therapy: female patients respond more readily than male.

The use of dried ovarian extracts is one of the most common forms of organotherapy. I venture to say that most gynecologists use this repeatedly in practice with a definite assurance of results. It is logical to use this substance in the menopause, which is evidently due to ovarian deficiency, and especially in the artificial menopause. There are no adequate statistical data as to the actual results. Desiccated corpus luteum is probably more valuable. In large doses it is useful in checking the vomiting of pregnancy. The intravenous use of corpus luteum extracts also gives definite results. The intravenous administration of ovarian extract and corpus luteum extract is distinctly useful in checking the nervous and psychical symptoms which are common at the menopause.

Organic products are useful in functional disturbances of menstruation when we can recognize a deficiency clinically: a thyroid deficiency indicates the use of thyroid extract, a pituitary deficiency indicates the use of pituitary extract, but the results in functional gynecological symptoms where a specific deficiency cannot be recognized are not so definite. Judgment

as to the efficacy of ovarian and corpus luteum extracts in functional menstrual disturbances must still await controlled statistical data

Adrenal cortex is a remedy which has recently been introduced for hyperthyroidism, based on the fact that it has been demonstrated that an increased metabolic rate results from injury to the adrenal cortex. While the results of this form of therapy are distinctly encouraging, it still awaits statistical proof.

The use of orchic and testicular extracts is logical in the symptoms of premature senility in males—what we might term the masculine menopause—and in frank eunuchoidism. But the actual effects of these substances must still be regarded very critically in spite of the fact that the specific deficiency is rather easy to recognize.

The use of thymus extract is still in the experimental stage and the same may be said for pineal extract.

Parathyroid extract is in common use, but we cannot as yet state whether it produces definite results or not. The latest work on the physiology of the parathyroids seems to indicate that their function is not hormone production, and consequently, the administration by mouth of parathyroid extract may not prove useful.

PHARMACEUTICAL PRODUCTS OBTAINED FROM THE DUCTLESS GLANDS

Within the past two decades, there have been isolated a number of specific substances from the ductless glands: adrenalin from the adrenal medulla and pituitrin from the posterior lobe of the pituitary gland. These substances produce unquestionable and definite pharmaceutical effects. Adrenalin is a powerful vasoconstrictor, it is able to relieve specific attacks of bronchial asthma, and recently it has been demonstrated that injections of adrenalin relieve the cramp-like pains of gastric ulcer. Pituitrin is a powerful uterine and involuntary muscle stimulant, it is a specific for diabetes insipidus. The pharmacologic effect of these substances has led to the deduction that they are secreted into the blood stream. While we have no such positive proof, it is distinctly justifiable to assume that similar substances, or mother substances, may be present in those glands.

which produce such effects in the normal physiology of the individual.

Thyroxin is an important and potent substance which has recently been isolated from the thyroid gland and produces powerful and definite effects in thyroid deficiency and is capable of elevating the basal metabolic level. The recently described substance insulin, which was obtained from the islands of Langerhans of the pancreas, has been shown to reduce diabetic hyperglycemia both in dogs and men.

The use of placental, mammary and other extracts is still in the experimental stage.

PLURIGLANDULAR THERAPY

It is apparent that in many endocrinopathies there is evidence of disturbance in more than one ductless gland, and in many instances there is evidence of pluriglandular deficiency. Nevertheless, it seems to me highly unscientific to prepare shotgun combinations of gland substances in the hope that the body will extract from these combinations those that it needs. The only way progress will ever be made in rational organotherapy is to be able to recognize specific deficiencies and to supply effective substances for these deficiencies. If more than one deficiency is present they should be individually recognized and two or more corresponding substances given.

While organotherapy still has definite shortcomings, it has, nevertheless, established the substitution principle of therapy. It has developed, within two decades, possibly five distinct new and reliable therapeutic agents. Several others give sufficient promise to warrant careful study.

But organotherapy is by no means unique in its shortcomings. The literature on therapeutics in general is remarkable for the paucity of systematized, controlled data on the efficacy of even the simplest remedies. The iodides, the bromides, the salicylates, and the vast group of coal tars, are used daily to the extent of tons, and the only effects obtained are for the large part subjective.

With the exception of the advances made in specific bacteriocidal and antitoxic therapy, progress in drug therapy has lagged. With the past two decades the only major advance has been the development of salvarsan and arsenic preparations,

which are distinctly useful in the relief of the first and second stages of syphilis and the specific gummatous syphilitic condition of the third stage. The effects on syphilitic endarteritis, aortitis, or aneurysm, paresis or tabes, give problematical subjective results, and very little, if any, objective result. Yet no one questions the use of antiluetic treatment for these conditions. Similarly, in the pituitary deficiencies it is logical to use the best preparations of pituitary extract that we have at hand, and although it is rare to get a marked objective result, it is, however, possible in a very large percentage of the cases to obtain relief of the symptoms that the patients actually suffer from. Such therapy is harmless and is far less deserving of criticism than the use of poisonous coal tars with the sole object of relieving subjective symptoms.

CONCLUSION

I have attempted to summarize the positive contributions that endocrinology has made to clinical medicine. Special limitations preclude covering the entire field, and I have attempted to present only the outstanding facts. I have stressed the positive findings because the negative findings have been so thoroughly stressed by others. I am quite conscious of the shortcomings of endocrinology, but these are merely in line with the shortcomings of medicine in general. They are not specific for endocrinology. The future of endocrinology is pregnant with progress, but it requires careful and critical study by investigators interested only in the search for truth. The opportunities for investigation lie both in the clinic and in the laboratory. As Dr. Barker has pointed out, in his chairman's address at the symposium on endocrinology at the last meeting of the American Medical Association, some laboratory workers seem to think that their field alone can develop truths and that the clinician can only develop errors. It must be borne in mind, however, that there are just as many possibilities for error in the laboratory as in the clinic. Laboratory experiments have a limited value and until now they have consisted largely, in the field of endocrinology, of the ablation and feeding experiments. Such experiments have their inherent limitations. It must also be remembered that experimental efforts to solve clinical problems are valuable if they produce positive findings that can be corroborated. Negative

results of animal experimentation can not be crucial. They merely establish some degree of antecedent doubt as to what may be found clinically if the conditions of the experiment are similar to those of the clinical state.

The positive achievements which I have attempted to outline certainly indicate that endocrinology has a definite place in medicine, and that it has contributed more than its proportionate share to the advancement of clinical medicine and therapy. It has shortcomings, which are no more than the shortcomings of medicine in general today. It is a branch of medicine that is worthy of the serious investigation of the best clinicians and the best laboratory workers. But progress can most rapidly be made when both clinician and laboratory worker have only one object—the search for truth. Both must appreciate the positive contributions as well as the negative and questionable data of the other.

Book Reviews

DISEASES OF THE THYROID GLAND Arthur E Hertzler, with chapter on hospital management by Victor E Chesky St Louis, 1922 C V Mosby Co 245 p 8°

Unlike many monographs, this book comprises very largely the personal experience of the author. This lends it unique value as well as leads to some conclusions that many surgeons will dispute. The study is based on many years of work with a somewhat localized group of patients, and opportunities for effective follow-up work have been unusual. Possibly for this reason the author is by no means enthusiastic as to the ultimate results of thyroid extirpation. "The best that can be said of the operative treatment," he writes, "is that it is the best we have to offer the patient. Fewer patients succumb from the operation than from the disease untouched."

He does not believe in the existence of "innocent goitres" but that, although they may exist for ten to forty years, they usually ultimately kill by undergoing toxic or malignant degeneration. "Personally, I categorically refuse," he says, "to treat colloid goitre—other than by operation."

The author is particularly to be commended in that he eschews the dubious term "hyperthyroidism" for the various sorts of thyroid intoxication. His use of words, in some other instances, however, is unfortunate. The constant use of "she" as generic for goitre patient is more or less of a libel. He also says he "operates" his patients—a fact which his reputation renders very doubtful. He even operates "cases." Such shop jargon has no place in a book so carefully written. The interpolation of bibliographic references immediately in the text is distracting.

Another unfortunate feature in the work is the publication of numerous mediocre photographs by way of illustrations. This practice, which is by no means uncommon, seems to be adopted on the supposition that the subjective element is thereby eliminated, it being forgotten that in the selection of specimens to photograph a high degree of subjectivity is inevitable. A comparison of the excellent drawings in the latter part of the book with the reproduced photographs brings out strikingly the inferiority of the latter.

The use of a high gloss, thick paper is annoying both to the retina and to the fiduciary consciousness of the reader

So much for adverse comments. They are of minor importance when compared with the many excellent features. The book as a whole is readable, and in some places, delightful for its racy diction. It is one which can be highly recommended, both as a repository of the wisdom of an experienced and careful student of goitre and as one the reading of which is a pleasure rather than a task. To the surgeon, of the technical aspects of the book, the graphic presentation of the art of thyroidectomy under local anesthesia will perhaps most appeal.—R G H

A PSYCHOANALYTIC STUDY OF PSYCHOSES WITH ENDOCRINOSES
Dudley Ward Fay. Washington, 1922. Nervous and Mental Disease Publishing Company. 122 p. 8°

The author reports a study of the case histories of 22 male patients afflicted with psychoses, either pure schizophrenia or other psychoses with schizophrenic features. These were selected cases with endocrine involvement, mostly "submyxedema." The book is taken up very largely with Freudian psychopathology. Not enough endocrine data are included to permit a satisfactory judgment as to the presence or absence of endocrine features. The endocrine material administered was, for the most part, desiccated thyroid gland. In one or two instances, this seemed to increase the troubles, but as a rule the effect appeared to be beneficial in varying degrees. One gets the impression that the actual effect was to increase the available energy of the patients and to give them a feeling of being more competent to cope with their environment. The beneficial effects appeared to be temporary, although in one instance the immediate benefit was spectacular.

In view of the paucity of endocrine data, the study cannot be regarded as of very great value as tangible evidence. It does indicate that the problem as studied is worthy of much more extensive investigation. The author feels that a combination of thyroid stimulation and psychoanalysis may prove an excellent method of attacking incipient schizophrenia.—R G H

EXOPHTHALMIC GOITER. Walter Edmunds, London, 1922, 2d ed
Ballière, Tindall & Cox. 36 p.

This little book embodies a lecture delivered at a London postgraduate college in 1921. It may be recommended to general practitioners who care to read a brief account of modern views on Graves' disease. Edmunds states that the secretory nerves of

the thyroid arise from the middle cervical ganglion. However, in most cases man has no middle cervical ganglion, but only a ganglion supremum and stellatum —J K

LE GOITRE ENDEMIQUE Dr F Messerli, Lausanne, 1916 Editeur, E Frankfurter 179 p

The author concludes that no relation exists between goiter and the geological constitution of the country. He attributes goiter to an infection of the water with a specific micro-organism and even describes a culture-medium to cultivate the virus. Goiter is caused not only by the drinking water, but also by contact, by the stools, by the sputa, etc. Modern experiments have not yet sustained this theory —J K

DIE LEHRE VON DER INNEREN SEKRETION E Gley Bern & Leipzig, 1920

A translation of Prof Gley's well known monograph into German, by Dr A Lipschutz. For review, see *Monatschr f Kinderh* (Leipz), 1922 22, 715 —R G H

DIE MASTURBATION Hermann Rohleder Berl, 1921 384 p

Among other topics the author discusses endocrine relationships. For review, see *Monatschr f Kinderh* (Leipz), 1922, 22, 720 —R G H

BASAL METABOLISM ITS DETERMINATION AND APPLICATION Edited by Frank B Sanborn, Boston Sanborn Co 282 p

A series of reprints of original articles by authorities on various aspects of basal metabolism —R G H

SENESCENCE THE LAST HALF OF LIFE G Stanley Hall, Ph D LL D D Appleton & Company, N Y, 1922 518 p

This book is an admirable presentation of the *raison d'être* of old age. In it is given the youth of old age, or the climacteric, the history of old age, literature by and on old age, statistics of old age and its care, medical views and treatment of old age, the contributions of biology and physiology to the understanding of old age, the answers to a questionnaire sent out by the author to oldsters, the conclusions drawn from the observations of the author and an excellent chapter on the psychology of death.

The part played by the incertitudes in the changes incident to the onset of the last half of life and their participation in the ultimate disintegration are rather sketchily given. Hall leans toward the Freudian psychology to the extent that he states, "I think I would gladly offer myself as a *corpus vile* for the Sternach operation to study its psychological effects at first hand." His philosophy of death is eminently materialistic.—F S H

Abstract Department

A function of the ADRENAL cortex (Ueber eine Funktion der Nebennierenrinde) Adler (L.), München med Wchnschr, 1922, 69, 797, Klin Wchnschr (Berl), 1922, 1, 1281

A dried adenoma of adrenal was given to tadpoles. The animals showed a tremendous growth and only male animals (at least when frogs were used) developed —J K

Correlation of ADRENAL weight with fetal development (Gli indici ponderali dei surreni in funzione della lunghezza e del peso del prodotto di concepimento) Cazzaniga (A.), Sperimentale Arch di biol (Firenze), 1922, 76, 121-129

The author has studied the growth curve of the human adrenal before birth, considering biometrically the absolute weights and the correlation weight index with the stature and the body weight together with the average deviation. He found that in the last month of pregnancy there is a retardation of increase in the fetal length and weight, and at the same time a marked augmentation of the suprarenal weight. During this period the growth of the body is not under the direct influence of these glands. At this time the nerve fibres undergo marked development and lipid grains appear in the pulmonary alveoli. It would seem probable that this latter phenomenon and the myelinization of the nerve fibres are correlated with lipid metabolism in the adrenals —P M N

An indistinct or atypical form of so-called ADRENAL VIRILISM (Formes frustes du virilisme dit surrénal) Claude (H.), Encéphale (Paris), 1921, 16, 491-495

The author has observed a large number of cases of virilism which he designates "formes frustes" because the physical and psycho-sexual disturbances are little in evidence and because the glandular (endocrine) dysfunction is in general not apparent. It appears that in this type of virilism the dystrophía may be brought about in the absence of tumors of the suprarenals by lutein hyperplasia in the ovaries with secondary reaction on the suprarenals. Since lutein cells as well as the cells of the suprarenal cortex are derived from the wolffian body, he suggests that wolffian virilism might be used instead of suprarenal virilism. One case is given in detail. In this patient sexual precocity began at the age of 7. At the time of puberty (at age of 11) a physical and moral change

occurred. She became timid and reserved. At the age of 18 a growth of hair appeared on her face and in other ways she began to change towards the masculine type. When examined at the age of 37 she was melancholiac. The mental disturbances were apparently secondary to the organic. There was sexual frigidity and very irregular menstruation. Biological tests indicated insufficiency of the thyroid and slightly of the suprarenals. Under treatment she improved. No literature given —A T R

The action of ADRENIN on the leucocytes and erythrocytes Cowie (D M), *Contrib Med & Biol Research (Osler)*, 1919, 2, 829-844

Cowie reports that the injection of adrenalin causes an initial rise in the leucocytes followed by a decline within one hour. At the second hour a further rise occurs and may last eight hours. All varieties of leucocytes participate. The red cells show similar rises. In both cases these are interpreted as being purely mechanical in origin —*Med Sc*, 1921, 3, 392

Observations on the functional activity of the SUPRARENALS in health and disease Cramer (W), *Scient Rep Imp Cancer Research Fund (Lond)*, 1919, 6, 1-21

Experiments mostly on mice, rats and rabbits show that the suprarenal gland and in particular the medulla is profoundly affected in a number of conditions (exposure to cold, fever and bacterial infections) associated with disturbances in the heat regulating mechanism. Changes in the functional activity of the medulla of the suprarenals, as evidenced by histological demonstration of adrenalin granules, were also observed in experimental hyperthyroidism, experimental acidosis, severe hemorrhage, anaesthesia and post-operative shock. In some cases there were also changes in the medulla of the suprarenals and in the thyroid gland. These observations are considered to be further evidence in support of the idea that the thyroid and suprarenals form a heat regulating apparatus which supplements the nervous mechanism. How this apparatus probably operates is discussed. The practical bearing of these points on specific treatment of certain conditions is brought out. The article is well illustrated. Twenty-one references are given.

—A T R

On the simultaneous effects of ADRENALINE and papaverine in the human organism (Hungarian) Csépai (K), *Orvosí hetil (Budapest)*, 1921, 65, 153-160

The antagonistic effects of adrenaline and papaverine on the blood pressure in dogs are confirmed. In man, however, papaverine enhances the pressor effect of adrenaline. The use of papaverine instead of pituitrin, in combination with adrenaline, is recommended for therapeutic purposes —*Physiol Abst*, 7, 133

ADRENAL ablation in epilepsy (*Nebennierenentfernung bei Epilepsie*) Engelbrecht (v), Klin Wchnschr (Berl), 1922, 1, 1282

A short note Operation did not improve the epilepsy—J K

Habitual vomiting and ptyalism of pregnancy treated with ADRENIN (*Vomissements tenaces de la gestation, ptyalisme traités par l'adrénaline*) Favreau, Soc de méd et de chir de Bordeaux, 1922, abst, J de méd de Bordeaux, 1922, 94, 430

Favreau reports the case of a woman of 27 who had been habitually constipated since her second pregnancy and who was troubled with frequent vomiting Her general condition was precarious, the urine was scanty, turbid and bile-colored There was also continuous ptyalism Since cold drinks did not help the constipation adrenin was prescribed Five days later the vomiting was diminished and 8 days after the beginning of the treatment there was neither vomiting nor salivation—R G H

Influence of ADRENIN in man (*Über die Gefasswirkung des Adrenalins beim Menschen*) Fornet (B), Arch f exper Path u Pharmacol (Leipz), 1922, 92, 165-172

The statement of Straub and Ritzmann, that of adrenaline injected subcutaneously only 6% reaches the blood stream, is not true for human subjects If adrenaline is injected intravenously into the forearm after a ligature has been previously applied to the arm so that the pulse is obliterated distal to the ligature, and if 10 minutes after the intravenous injection the ligature is removed, the typical adrenaline action takes place The author considers that this proves that adrenaline is not destroyed in the blood stream Neither is adrenaline destroyed in the subcutaneous tissues

—Physiol Abst, 7, 258

The antagonistic action of caffeine and ADRENIN on the isolated intestine (*Action antagoniste de la caféine et de l'adrénaline sur l'intestin isolé*) Fredericq (H) & Mélon (L), Compt rend Soc de biol (Par), 1922, 87, 92-94

The action of caffeine on the isolated rabbit intestine is antagonistic to that of adrenalin Caffeine causes the tonus and contractions which have been abolished by adrenalin to reappear Adrenalin, on the other hand, reduces the augmented tonus produced by a previous treatment with caffeine Caffeine, therefore, acts as an antagonist to the sympathico-mimetic action of adrenalin—W B C

Influence of ADRENAL, HYPOPHYSIS and PINEAL feeding on cutaneous pigmentation and respiratory rhythm of Salmo fario (*Influenza dell'alimentazione con capsule surrenali, ipofisi ed epifisi su la pigmentazione cutanea, ed il ritmo respiratorio di "Salmo fario"*) Gianferrari (Lulsa), Arch di sc biol (Napoli), 1922, 3, 39-52

The author has studied the young fry of *Salmo fario*, because the action of nerves on the pigmentation is well known, because these fish are subject to rapid variations of cutaneous color, and it is easier to determine the modifications of increase of blood in the gills, in relation to the modification of the respiratory rhythm. Whether the fry are fasted or fed with plankton or with spleen the results are the same. Animals in five receptacles were fed respectively adrenal medullary substance, adrenal cortex, adrenal whole gland, hypophysis and pineal of the horse. Only a few ate the medullary substance. Those that did so lost the color of their skin in four or five hours, remaining yellowish-white for two days, on the fourth day they were almost all repigmented. Those that refused to eat the substance retained their normal color. The depigmentation began with a band behind the gills, and thence extended over the whole body. The author concluded that the phenomenon depended on the material ingested and not on glandular substances dissolved in the water which acted externally, since some were put into a receptacle with clean water as soon as they had eaten and lost their color the same as the others. Together with this depigmentation they presented dyspnoea, the gills appeared turgid, hyperemic and with larger spaces between the gill arches, they remained stationary at the bottom of the receptacle. When the color came back all the other symptoms disappeared. If, after having recovered their normal state, they again ate adrenal substance, they were subjected to the same modifications, but before recovering their normal color they died. Eating cortical substance alone did not cause any alteration except in case of a few animals that probably obtained a small amount of medullary substance with the cortical preparation. Hypophysis feeding caused depigmentation of less intensity but longer duration than did adrenal feeding. Pineal feeding gave a similar effect, but it did not produce any action on respiration. These experiments indicate that contraction of the chromatophore cells is determined by the sympathetic system, since adrenalin acts selectively on this system and hypophysis and perhaps the pineal have some connection with it.—P M N

The action of ADRENIN on the blood picture in leukemias (L'action de l'adrénaline sur le tableau leucocytaire dans les myéloses)
Goia (J), *Presse méd* (Par), 1922, 30, 366-369

Goia studied the effect of injections of adrenalin in pathologic conditions of the blood on two cases of myelogenous leukemia, two cases of (lymphocytic) pseudoleukemia and in one splenectomized patient. He used 0.001 (cc?) of "Tonogen" Richter, subcutaneously. Blood counts were made 10, 20, 30 and 60 minutes as well as 3 and 6 hours after injection. He found that in myelogenous leukemias the total leucocyte count rose from 380,000 to 460,000 at the end of 10 minutes and to 580,000 at the end of 20 minutes, by a rapid in-

crease of myelocytes and myeloblasts, the lymphocytes showed a slight increase at first, but later a marked reduction in numbers. In pseudoleukemias the leucocytic reaction was the result of a rapid increase of the lymphocytes. In chronic myelogenous leukemias in which very few myelocytes and myeloblasts were found in the blood before injection, the leucocytosis was again predominantly myelocytic. After splenectomy the leucocytosis was also marked, but the lymphocytes as well as the myelocytes and the polymorph neutrophils increased. Goia concludes that the reaction to adrenalin shows a stimulation of tissues capable of response, either lymph nodes and spleen or bone marrow. The hypertrophy of the marrow with retrogression of the lymph glands explains the myelocytic reaction in myelogenous leukemia, the intact condition of the lymphoid elements in pseudoleukemia, the predominance of the lymphocytic reaction in the latter. He suggests that injections of adrenalin may be of value to establish the differential diagnosis, which is often difficult in cases of chronic myelogenous leukemia and pseudoleukemia.

—G L

The mechanism of hyperglycemia after the injection of ADRENIN
(*Untersuchungen über den Mechanismus der Adrenalinhyperglycämie*) Gottschalk (A) & Pohle (E), *Klin Wchnschr* (Berl), 1922, 1, 1310-1311

Continuous intravenous infusion of a diluted solution of adrenalin or subcutaneous injection of enough to produce hyperglycemia produces a very marked rise of the hydrogen ions and concentration of the blood in the vena porta and vena hepatica. This rise reaches its maximum in the capillaries of the vena porta. If a quantity of alkali is first administered, hyperglycemia is much less marked. Therefore, the authors conclude that increased acidity of the blood is a "conditio sine qua non" for adrenin hyperglycemia.

—J K

Epithelial tumor of the ADRENAL (*Epithelialer Tumor der Nebenniere*) Horner, *Deutsche med Wchnschr* (Berl), 1922, 48, 886

No details are given —J K

(ADRENIN) Hyperglycemia in diseases with hypertonia (*Zur Frage der Hyperglykämie bei Krankheitszuständen mit Hochdruck*) Kahler (H), *Wien Arch f innere Med*, 1922, 4, 129-148

Kahler could not confirm the view of many investigators that there is hyperglycemia in all cases of hypertonia. Many patients with high blood pressure have a perfectly normal quantity of blood sugar. Hyperglycemia, however, is very often found when there are complications, as in apoplexy, eclampsia or uremia, it is also found in "essential hypertonia" with sclerosis of the vessels of the pancreas and in cases with stasis of the blood. When adrenalin is injected in patients with a high blood pressure, the effect is just the

same as in normal persons This fact and the fact that in a large number of patients with hypertonia there is no hyperglycemia make it improbable that hyperadrenalinemia is the cause of hypertonia When a high blood pressure is complicated by stasis of the blood there is always hyperglycemia It is possible, but not probable, that this is caused by hyperadrenalinemia—J K

Histochemistry of melanin and ADRENIN (*Histochemie des Melanins und des Adrenalins*) Kutschera (H), Wien klin Wchnschr, 1922, 35, 554

Ammoniacal silver nitrate may be reduced in vitro by catechol and in the tissues by melanin and adrenalin In the liver, heart and adrenals a pigment (lipofuchsin) is found which, after its fats are extracted, also reduces ammoniacal silver nitrate Lipofuchsin is probably melanin, surrounded by lipoids Adrenalin finds its origin in the protoplasm of the cells of the medulla of the adrenals, some times transported into the cortex The capillaries of the cortex have communications with the veins of the pancreas The chromaffin substance is very sensitive to some substances It is destroyed by prussic acid, by heat and by cold From this we may conclude that the chromaffin substance has some properties in common with the enzymes As this is not the case with adrenalin, the chromaffin substance is not identical with adrenalin, but may play a certain rôle in its formation—J K

Blood pressure after the injection of ADRENIN in hypertonia (*Adrenalinblutdrucksreaktion bei Hypertonisten*) Kylin (E), Zentralbl f innere Med (Leipz), 1922, 43, 329-331

Some time ago Kylin pointed out that the blood pressure is often high in diabetes, especially in elderly persons He therefore believed that there might be a certain relation between the endocrine disturbances in hypertonia and in senile diabetes He injected 1 mg of adrenalin subcutaneously in healthy persons and in patients The blood pressure curve in acute nephritis is the same as that in healthy persons In 14 cases of hypertonia from benign sclerosis of the kidney 13 patients showed an abnormal reaction During the first 15-20 minutes after the injection the blood pressure may sink 40-50 mm, rising again to its original height or even higher This abnormal reaction makes it highly probable that endocrine disturbances have some relation to the pathogenesis of benign sclerosis of the kidney and to hypertonia—J K

Gastric crises and paroxysmal hypertension related to an ADRENAL tumor (*Crises solaires et hypertension paroxystique en rapport avec une tumeur surrénale*) Labbé (M), Tinel (J) & Doumer, Bull et mém Soc méd des hôp de Par, 1922, 46, 982-990

A characteristic detailed case report of paroxysmal neural crises, of epigastric constriction, nausea, vomiting and vaso-motor disturb-

ances accompanied by arterial hypertension and terminating fatally. At autopsy the left adrenal was found to have been replaced by a tumor the size of a large mandarin orange, and having the medullary structure of the adrenal. The other endocrine glands seemed normal in size. The thyroid section showed evidence of heightened activity. The relation between this probable hyperepinephrinemia and the arteriotrem symptoms is stressed.—F S H

Malign neuroblastoma of the sympathetic in the right ADRENAL
(Ein malignes Neuroblastom des Sympathicus in der rechten Nebenniere) Lauche, Klin Wchnschr (Berl), 1922, 1, 1233

No details are given except that a girl of 3½ months had a tumor with metastasis in the liver.—J K

(ADRENAL) Thomsen's disease of amyotrophic type (Maladie de Thomsen fruste à type amyotrophique) Lecaplain & Billard, Normandie méd (Rouen), 1922, 33, No 3, abst, Presse méd (Par), 1922, 30, 492

A case is described of Thomsen's disease of amyotrophic type. The syndrome is progressive, bearing always upon the extremity of the superior members and accompanied by slight signs of adrenal insufficiency. There are also signs of degeneracy, but with familial character. This case is comparable to an observation recently published by Roger and Aymès.—R G H

The influence of ADRENIN on the ocular pressure and on the blood pressure, general and retinal (De l'influence de l'adrenaline sur la tension oculaire et sur la tension sanguine générale et rétinienne chez l'homme) Leplat (G), Ann d'ocul, 1921, 158, 414-423

Injection of adrenaline produces a rise of pressure in the central retinal artery parallel to that produced in the general arterial system, rise of intra-ocular pressure was not observed. Instillation of adrenaline leads to a slight fall of intra-ocular pressure with no change of retinal arterial pressure. Changes of intra-ocular pressure are independent of changes of retinal venous pressure.

—Physiol Abst, 7, 259

Is ADRENIN a hormone (È l'adrenalina un ormone)? Marfori (P), Arch intern de pharmacod et de thérap (Brux), 1921, 26, 137-149

A critical and experimental publication directed to the examination and the interpretation of Gley's experiments, denying not only the harmonic character of adrenalin but also every other normal function in the organism. Marfori has demonstrated that if from an animal with high blood pressure—caused by injection of the minimum of adrenalin sufficient to produce some effect—we

take 30 or 40 cc to reinject in the same animal after it has become normal or in another animal in good health, there is no modification in blood pressure. A minimum of adrenalin in the blood is necessary to manifest its action. It is probable that in Gley and Quinquaud's experiments the adrenin was insufficient to produce definitely increased blood pressure. The problem as to the hormonal nature of the endocrinal products cannot be solved with only physiological or pharmacological experimentation, but anatomical, pathological and clinical data must also be considered —G C

Partial ADRENAL deficiency (*Ueber einseitigen Nebennierenmangel*) Miloslavich (E), *Zentralbl f allg Path u path Anat* (Jena), 1920, 30, 465-470

Developmental disturbances of the adrenals have been observed chiefly in non-viable infants and are usually associated with serious defects of the central nervous system. Miloslavich has collected 8 cases of absence of one adrenal in children and adults and adds one case of his own. His patient was a 72-year-old female dwarf. There was complete absence of the right kidney, right adrenal and no trace of the renal and adrenal arteries on the right side could be found. There were, further, malformations of the intestine and polydactylism of both hands and feet. In all of the cases collected from the literature it was the right adrenal that was absent —J P S

Effects of ADRENALECTOMY on the automatic contractions of the isolated duodenum of the rabbit (*Effets de la l'ablation des surrénales sur les contractions automatiques du duodénum isolé du lapin*) de Mira (F) & Fontes (G), *J de physiol et de path gén* (Par), 1921, 19, 1-12

The spontaneous contractions of the excised duodenum of rabbits, from which the adrenals have been removed, are very small or absent. The effect is present even in an hour. Controls show that it is neither due to anesthetic nor to shock. The inhibitory reaction to adrenalin is apparently unaffected. Adrenalin itself was unable to supply the deficiency of the whole adrenal. The injection of adrenal extract after the removal of the adrenals, prevents the appearance of inactivity in the duodenum fifteen minutes after the injection. It is suggested that the cortex is responsible.

—Physiol Abst

Surgery of the ADRENALS (*Grundsätzliche Fragen in der Chirurgie der Nebennieren*) Peiper (H), *Klin Wchnschr* (Berl), 1922, 1, 161-163

Removal of an adrenal has been recommended by Stephan in polycythemia and by Fischer and Brunings in epilepsy. There have been no definite results in this operation in polycythemia up to this time. The great difficulty in the surgery of the adrenal is com-

pensatory hypertrophy, but this is not constant One adrenal was removed in a very severe case of epilepsy, but operation had no effect Ten months later the patient died of typhus At the post-mortem examination no trace of hypertrophy of the other adrenal was found—J K

The lipid content of the ADRENAL cortex of the guinea pig in experimental scurvy (Über den Lipoid-gehalt der Nebennierenrinde des Meerschweinchens bei experimentellem Skorbut) Peiper (H), Klin Wchnschr (Berl), 1922, 1, 1263-1264

When guinea pigs die from starvation or cachexia the cortex of the adrenals contains large amounts of lipoids When they die from experimental scurvy, little or no lipoids are found If vitamine C is given to animals with scurvy the adrenals (first the outer layers of the zona fasciculata) become very rich in lipoids—J K

(ADRENIN) Action of blood, plasma, red cells, normal and asphyxiated, on the isolated intestine (Action du sang, du plasma, des globules rouges normaux et asphyxiés sur l'intestin isolé) Pellegrini (R), Arch internat de physiol (Liège & Par), 1921, 17, 209-226

The author does not admit the existence of adrenalin in normal circulating blood, but frequently finds in whole hirudin-treated or fibrinated blood, in the plasma, in the red cells and in the serum, substances having a tonic action on the intestine These substances are thermolabile Asphyxia increases them Physiol Abst, 6, 582

(ADRENIN) Influence of light rays on carbohydrate metabolism (Über die Beeinflussung des Stoffwechsels der Kohlehydrate durch Strahlung) Pincussen (L), Klin Wchnschr (Berl), 1922, 1, 174

When a rabbit is exposed to light rays and adrenalin is injected the blood sugar is much higher than after a simple injection Light rays after injection of eosin decrease the blood sugar When the rabbit gets eosin first, is exposed afterwards to light rays, and then gets adrenalin, the blood sugar is raised, but not so much as it is in the animals which did not receive eosin In diabetes it is often possible to diminish the blood sugar markedly after injection of eosin, even the acetone bodies sometimes disappear from the urine In hypophyseal diabetes (with polyuria) light rays have no effect —J K

The action of atropin, ADRENIN, and pilocarpin (Zur Wirkung des Atropins, Adrenalins und Pilocarpins) Platz, München med Wchnschr, 1922, 69, 727

Atropin was given in doses of 0.05 to 1 mg When the dose is less than 0.5 mg the pulse becomes slower When larger doses are

given intravenously the pulse rate at once increases, when given subcutaneously there is first bradycardia, followed by tachycardia. Adrenalin was injected into 121 patients. Even 0.001 mg given intravenously produces a marked rise of blood pressure. The increase of the blood pressure does not parallel the quantity of adrenalin injected. In 116 of the 121 patients adrenalin caused an increased pulse rate. After intravenous injection respiration is quickened and the blood sugar and NaCl in the blood is increased. Erythrocytes and leucocytes are increased along with neutropenia, eosinophilia, and lymphocytosis. The mononuclears may be increased or decreased. General symptoms, such as headache, giddiness and paleness are much more marked after intravenous than after subcutaneous injections. Even 18 mg of adrenalin given intrarectal have no effect. Pilocarpin always increases the pulse rate and causes the blood pressure to sink and the blood sugar to increase —J K

The influence of pilocarpin, ADRENIN and atropin in the study of the involuntary nervous system (*Die Wirkung des Pilocarpins, Adrenalins und Atropins als Beitrag zur Prüfung des vegetativen Nervensystems*) Platz (O), *Klin Wchnschr (Berl)*, 1922, 1, 1230, *Deutsche med Wchnschr (Berl)*, 1922, 48, 788

Pilocarpin, adrenalin or atropin may have quite different effects according to whether they are injected subcutaneously or intravenously. For the pharmacological study of the irritability of the vegetative nervous system, it is best to inject them directly into the veins. However, their action is often too severe if this method is used —J K

Lesions of the vessel-walls caused by ADRENIN (*Sulle alterazioni delle pareti vascolari prodotte dall' adrenalina sia per iniezione in circolo, sia per contatto*) Poletti (B), *Arch per le sc med (Torino)*, 1920, 43, 63-92

Repeated intravenous or intraperitoneal injections of fractional doses of adrenalin, constantly cause, in rabbits, aortic changes consisting of degeneration and necrosis of the plain muscle-fibres of the middle coat. These lesions are followed by distension, atrophy, fragmentation, and destruction of the elastic fibres. The degenerated places in the aorta become lastly extensively calcified. These alterations are identical with those found in the aortae of rabbits, the subjects of idiopathic arteriosclerosis, hence the conclusion that the arteriosclerosis of rabbits can be experimentally reproduced. If adrenalin is directly applied to the walls of arteries, such as the carotid or the femoral, lesions can be observed which do not essentially differ from those caused by injections of adrenalin. But if adrenalin is directly injected into the urinary bladder no lesions of the plain muscle-fibres are produced, but only haemorrhages per diapedes from the blood-vessels of the submucosa. These facts sug-

gest the conclusion that the arteriosclerotic changes caused by adrenalin are very likely due to a local and direct influence exercised on the muscle-fibres of the arterial walls and only in part or very little to the hypertension which follows the passage of adrenalin into the blood-stream. How it is that the influence of adrenalin is felt by the muscle-fibres of blood-vessels and not by those of the wall of the bladder remains as obscure as the selective action of certain drugs and other substances on determined cells or tissues.

—Med Sc, 1921, 3, 372

(ADRENIN) The treatment of uncontrollable vomiting (*Discussion sur le traitement des vomissements incoercibles*) Rathery, Soc d'obst et de gynec, 1922 (May 8), abst, Presse med (Par), 1922, 30, 480-481

Rathery describes the therapeutic results which he obtained in pregnant women (primiparae and multiparae) who, from the second month, had been in a serious condition due to incessant vomiting. Asthenia, very marked, was accompanied by a low temperature, by arterial tension of about 100/60 to 90/50 and by a very rapid pulse. The urine, which was much diminished, revealed the presence of acetone. Radioscopy showed gastric myasthenia. Adrenin was given in doses of 1-2 mg a day for 1-7 days. The author emphasizes the rapid action of the drug, vomiting ceases quickly, asthenia diminishes, the pulse rate is lowered, and the urinary acidosis disappears. If the adrenin administration is stopped Gerhardt reaction appears again in the urine. There is a very obvious relation between adrenin and acidosis. The action of adrenin is lasting—the author has never seen vomiting reappear. Rathery believes these good results are due to the action of the proper medicament rather than to a possible pluriglandular insufficiency.—R G H

Some technical points in the method of physiological control of **ADRENALIN** products. Richaud (A), J de pharm et chim (Par), 1922, 25, 289-298

The necessity of washing the adrenalin from the cannula after each injection by Cushny's control method is discussed. From the tracings obtained upon injecting, for comparison, solutions of unknown and known strengths of adrenalin, Richaud deduces the increase of blood pressure (which is a function of the adrenalin contents), by drawing the heights of the curves. A graph made from these increments as ordinates and the concentrations of the solutions used as abscissas, gives a direct means of comparison.

—Chem Abst, 16, 2385

Blood sugar in Addison's disease and the influence of ADRENIN (*Der Blutzucker bei Addisonscher Krankheit und seine Beeinflussung durch Adrenalin*) Rosenow (G), & Jaguttis, Klin Wchnschr (Berl), 1922, 1, 358-360

Most authors describe hypoglycemia as a classical symptom of Addison's disease, but in Addison's disease, just as in normal persons, the blood sugar varies decidedly, and it may happen that a patient may show hypoglycemia one morning and normal quantity of blood sugar the next day. For the diagnosis of "hypoglycemic Addison" it is necessary to determine the blood sugar for a number of consecutive days on an empty stomach. When adrenalin is injected into a patient with Addison's disease, the blood sugar rises, but to a much less extent than would be the case in normal persons. The maximum, just as in normal persons, is reached in ± 1 hour. Normal persons often show a secondary hypoglycemia after "adrenalin-hyperglycemia." This hypoglycemia was not found in Addison's disease.—J K

Hemoclastic agonal tabetic crises treated with ADRENIN (Crises algiques tabétiques hemoclasiques. Leur traitement par l'adrénaline). Sicard & Lermoyez (J), *Bull et mém Soc méd des hôp de Par*, 1922, 46, 797-801

The slow intravenous injection of 0.5 mg of adrenin in 10 cc of artificial serum into 3 tabetic patients gave relief when no other medication was effective. Improvement occurred in from one-half to two hours. The dose can be repeated after several hours.

—F S H

Unilateral ADRENAL ablation in man (Die Einseitige Entfernung der Nebenniere beim Menschen). Steinthal, *Klin Wchnschr* (Berl), 1922, 1, 1258-1260

Effect from operation in epilepsy was seen only in an infantile boy of 15, who had no attacks for over a year after the ablation of an adrenal. Why this boy was cured, or at least markedly improved is unknown. It has been repeatedly stated that ablation of one adrenal always gives rise to hypertrophy of the second, but this is not at all certain. Pelper has described a case in which at autopsy 10 months after the ablation of one adrenal there was no trace of hypertrophy of the second. Steinthal also reports a case in which the operation brought no good results and the patient died 10 months after the operation. At autopsy it was seen that the remaining adrenal weighed 10.5 gm whereas the adrenal that had been removed weighed 3 gm. (Simmonds, however, considers 10 gm to be a normal weight.) In the hypophysis a small zona intermedia and an under-developed pars nervosa were found, the thyroid showed a colloid goiter, the ovaries and the thymus showed nothing of especial interest.—J K

Are the practical effects of extirpation in hyperfunction of the ADRENALS local or in higher nervous centers (Welche praktischen Erfolge seitigt die Exstirpation bei Hyperfunktion der

Nebenniere selbst oder von deren zentral ubergeordneten Zentren)?
Stephan & Floercken, Klin Wchnschr (Berl), 1922, 1, 1128

In two cases of hypertonia ablation of an adrenal had no effect (only the number of erythrocytes was diminished) X-ray treatment of the adrenals causes atrophy of the cortex and has no influence on the chromaffin tissue —J K

Injection of ADRENIN in lunatics (Adrenalin proef inspuitingen bij geestesszleken) Stuurman (F J), Nederl Maandschr v Geneesk (Leiden), 1922, 3, 44-60

Subcutaneous injection of 0.7 mg of adrenalin causes an increased systolic blood pressure and an increased pulse rate. The diastolic pressure generally sinks or remains unaltered, in very rare cases it is increased also. Persons suffering with schizophrenia show a less marked reaction than other lunatics. The paranoiac form shows a more intense reaction than the catatonic or the hebephrenic forms. Epileptic patients show a diminished reaction of pulse and blood pressure, they often develop glucosuria. Manic-depressive patients show a rather intense reaction, especially the unquiet forms of melancholia, who generally have a high blood pressure. Administration of alkali diminishes the effect of adrenalin. It is probable that in melancholia adrenalin increases the anxiety. It is important, therefore, to try out the effect of alkali in this disease —J K

Extirpation of the ADRENALS in epilepsy (Über Nebennieren-exstirpation bei Epilepsie) Sultan, Klin Wchnschr (Berl), 1922, 1, 145

See Endocrin, 1922, 6, 535 —J K

(ADRENAL) Ethmoid-orbital metastasis of latent hypernephroma (Métastase ethmoïde orbitaire d'un hypernéphrome latent) Van Duyse & Marbaix, Brux Méd, 1922, 2, 423-425

A tumor was removed from the ethmoid showing the histological picture of hypernephroma. Though no clinical symptoms of a primary tumor were present, on the roentgenogram a large shadow was seen between the left kidney and the vertebral column, caused perhaps by a primary tumor —J K

Histological changes in the ADRENALS during pregnancy (Comment faut-il comprendre, au point de vue histologique, le fonctionnement des capsules surrénales au cours de la gestation 1re note)? Watrin (J), Rev méd de l'est (Nancy), 1920, 48, 349-353

Thirty-two out of 35 rabbits showed hypertrophy and evidences of hypersecretion in the cortical zone (medulla apparently not involved) which was already visible on the fifth day following fecundation. By the thirtieth day of pregnancy the suprarenal averaged more

than double, and was occasionally three times its normal size. Most of the increase was in the zona fasciculata due to an increase in the size of the cells and to encroachment upon neighboring zones. There was but little evidence of cell division—A. T. R.

(ADRENAL) A case of tumor of the fourth ventricle of the brain, accompanied by cutaneous pigmentation like that of Addison's disease. Weber (F. P.), *Internat Clin (Phila)*, 1922, 2, 93-101.

A girl of 14 was suffering with nervous restlessness, excitement, vomiting, rapid pulse, and irregular fever. She was emaciated, and there was considerable cutaneous pigmentation resembling that of Addison's disease. Laboratory reports were negative. Seventeen days after admission to the hospital the patient became stuporous, and death occurred 12 days thereafter. The pigmentation of the trunk had apparently increased while in the hospital. Autopsy revealed a tumor about the size of a large acorn, growing within the fourth ventricle of the brain. No evidence of disease of the suprarenal glands was discovered. The author suggests that the cutaneous pigmentation "may have been in some unknown way a result of the gliomatous disease of the brain"—I. B.

Influence of ADRENIN in different concentrations on blood pressure and blood sugar (*Adrenalinwirkung auf Blutdruck und Blutzucker bei verschiedener Konzentration*). Weinberg, München *med Wchnschr*, 1922, 69, 797, *Klin Wchnschr (Berl)*, 1922, 1, 1282.

Very small quantities of adrenalin cause the blood pressure to sink, large quantities produce a rise. When adrenalin is given intravenously, but so slowly that the injection takes ± 1 hour the blood sugar is diminished. No details are given—J. K.

Activity of sterilized and unsterilized ADRENALIN solutions
Wischo (F.) & Zechner (L.), *Arch Pharm*, 1921, 146-149.

The authors find that a solution of adrenalin-HCl is sensitive to both light (ultraviolet) and heat, that the demand for absolutely colorless solutions is unjustified, since rose to faintly red solutions show full activity, sterilization causes no diminution but may on the contrary effect an increase in the activity of the drug.

—Chem. Abst., 16, 787.

ADRENAL ablation in epilepsy (*Nebennierenexstirpation bei Epilepsie*). Wohlegmuth (K.), *Fortschr d Med (Berl)*, 1922, 40, 399-400.

A general review of the literature—J. K.

(ADRENAL) Surgical pathology of hypernephroma. Wright (L.), *Brit J Surg (Bristol)*, 1922, 338-365.

With Grawitz' hypothesis (1884), that these tumours arise from suprarenal rests, the author cannot agree, amongst the facts which

militate against this contention are the following Hypernephromata are not confined to any one area in the kidney, there is no adrenalin contained in these tumours, unlike the suprarenal tumours, alterations in sex characteristics have never been noticed in hypernephromata, no case of tumour in the suprarenal gland has ever been proved to have a papillary structure

—Irish J M Sc, 1922, 5 s, 80-81

Diagnosis of SUPRARENAL insufficiency Wright (S), Lancet (Lond), 1922, 2, 14, abst, J Am M Ass (Chicago), 1922, 79, 505-506

See Endocrin, 1922, 6, 493-510 —R G H

ADRENALIN tests Zechner (L) & Wischo (F), Pharm Monatsh, 1921, 2, 141-146

The number of adrenalin tests recorded in the literature is relatively large, involving for the most part oxidizing agents capable of developing a characteristic color The authors report results in experiments with FeCl_3 , KMnO_4 and $\text{K}_2\text{Cr}_2\text{O}_7$ For adrenalin solutions 1 100 and 1 1000, the optimum concentration and amount of FeCl_3 solution were 1 drop of a 50% and of 5% FeCl_3 solution, respectively, to 1 cc adrenalin solution, for all lower concentrations a drop of 0 5% FeCl_3 solution to 1 cc (for the concentrations 1 1,000,000 and 1 10,000,000, 6 to 10 cc) of the adrenalin solution, making a control test with a like amount of H_2O in the case of such high dilutions The optimum temperature for all concentrations was about 10 to 15° One drop of a 5% $\text{K}_2\text{Cr}_2\text{O}_7$ solution added to 1 cc of a 1 1000 solution produces a color range of yellow, orange and red, followed by a turbidity and finally brownish flakes The turbidity does not occur with 1 drop of a 0 5% $\text{K}_2\text{Cr}_2\text{O}_7$ solution With this strength of reagent, the test is sensitive to a 1 100,000 adrenalin solution In the case of KMnO_4 , 1 drop of a 0 1% solution gives a red color with adrenalin solutions, this test being sensitive in dilutions of 1 100,000 —Chem Abst, 16, 787

The BASAL METABOLISM and the specific dynamic action of protein in LIVER disease Aub (J C) & Means (J H), Arch Int Med (Chicago), 1921, 28, 173-191

The authors conclude that the basal metabolism in twelve cases of liver disease was essentially within normal limits The liver is therefore either not an important regulator of the metabolic rate, or it is adequate for this purpose even when severely diseased The rate of absorption and utilization of protein in large quantities was usually normal, even in severe cirrhosis In two cases of cirrhosis and one of gall stones, the utilization of the protein was delayed or absent Marked portal obstruction caused no delay in the appearance of the specific dynamic action of protein The cases of cirrhosis

showed, on the whole, the highest metabolic response to protein catabolism. The conclusion seems justified that either the liver is not the main site of the specific dynamic action of protein, or that it can adequately perform that function even in disease. The specific dynamic action of protein results from an increased combustion of protein and carbohydrate rather than fat. The observation of Du Bois that in exophthalmic goitre a normal increase in heat production, due to protein, is superimposed on the high basal rate is confirmed.—H L

Correlation of BASAL METABOLIC RATE with pulse rate and pulse pressure Read (J M), *J Am M Ass* (Chicago), 1922, 78, 1887-1889

Three hundred determinations form the basis for this report. Cases showing an obvious pathologic condition in the cardiovascular-renal system are not included. A formula is offered correlating pulse rate, pulse pressure and basal metabolic rate. Pulse rate and pulse pressure vary in the same direction as the basal metabolic rate and in most individuals the change is proportionate.—W M A

The pathology and treatment of DIABETES (*Bemerkungen zur Pathologie und Therapie des Diabetes mellitus*) Abderhalden (E), *Klin Wchnschr* (Berl), 1922, 1, 1089

In severe cases of diabetes the red corpuscles use only small quantities of oxygen. If, however, substances contained in yeast are added its use ("Sauerstoffzehrung") is largely increased. In avitaminosis the respiration of the cells (Zellatmung) is very low and yeast causes it to increase at once. Therefore, avitaminosis may perhaps play some part in causing diabetes. As the author is no clinician he suggests that medical men study this as possibly leading to useful treatment.—J K

(DIABETES) Variations in the blood sugar after intravenous injection of novarsenobenzol (*Les variations du sucre sanguin à la suite de l'injection intraveineuse de novarsénobenzol*) Achard (C), Binet (L) & Cournand (A), *Compt rend Soc de biol* (Par), 1922, 86, 714-717

Injection of novarsenobenzol in man with a normal blood sugar results in slight hyperglycemia. In diabetics and others with defective carbohydrate metabolism, it leads to a diminution of the blood sugar. Addition of novarsenobenzol to normal and diabetic bloods in vitro did not affect the sugar content.—*Physiol Abst*, 7, 251

(DIABETES) PANCREATIC extracts Banting (F G) & Best (C H), *J Lab & Clin M* (St Louis), 1922, 7, 464-472

By intravenous and subcutaneous injections of neutral saline extracts prepared from the pancreas of the bovine fetus at about the

fifth month, the percentage of blood sugar and the daily urinary excretion of sugar were markedly reduced in depancreatized dogs. Daily injections of extract of pancreas enabled a depancreatized dog to live for 70 days. A small remnant of pancreas was found, however, at autopsy. The active (antidiabetic) principle of such extracts is destroyed by boiling in strongly acid reaction, but it is not affected by the presence of tricresol which may therefore be used as a preservative. The depressor action of the extract is short-lived.—R G H

The liver is **DIABETES mellitus** Bate (R A), Am Med, 1918, n s 13, 220-226

A general article not amenable to abstracting. The author discusses various data bearing on the diabetes problem. These are largely elementary physiology and speculative endocrinology. He regards the liver and lungs as more or less similar in that both detoxicate the blood, both organs are under hormone control. In diabetes, dextrose never is stored in the liver. Trypsinogen, a hormone from the islands of Langerhans, and glycogen are always found where sugar combustion occurs. Possibly in prenatal life the thymus gland helps in the glycogenic function. Sugar piqûre is ineffective after adrenal ablation or splanchnic section. Possibly the pancreas hormone is neutralized by increased adrenal secretion. Then follows a review of various data on the parathyroids, spleen and hypophysis. Septic diabetes is mentioned in connection with a case of diabetes and bed-sores following fracture of the hip joint. A case of traumatic diabetes is also mentioned. For other details the original may be consulted. The therapeutic use of liver extracts in diabetes as well as in tuberculosis is advocated. At the author's request this abstract is substituted for one previously published.—R G H

A case of sudden pneumonia in a **DIABETIC** (Un cas de pneumonie foudroyante chez une diabétique) Bonnamour & Girardot, Bull Soc méd d hôp de Lyon, 1922, abst, Presse méd (Par), 1922, 30, 620

The authors report the case of a woman of 69 years who had had diabetes for 2 years, eliminating 3 litres of urine, with about 200 gr of sugar and traces of acetone in 24 hours. Although supposedly on a diet, she secretly ate a great variety of food. One morning she complained of a vague stitch in her side. Auscultation was negative. The next day she was in a state of cyanosis, collapse and hypothermia. The urine contained an enormous quantity of acetone and diacetic acid. She died the next morning. Autopsy confirmed the existence of severe pneumonia.—R G H

Incidence of **DIABETES mellitus** among Filipinos Concepción (I), Philippine Islands M Ass J (Manila), 1922, 2, 57-63, abst, J Am M Ass (Chicago), 1922, 79, 502

Concepcion shows that the mortality of diabetes mellitus in the city of Manila has apparently been increasing within the past few years, but this is due to a greater accuracy of vital statistics. There is no reason to believe that increased consumption of sugar is one of the main factors. The incidence of diabetes in the Philippines is very much less than in other countries, including Japan, despite the use of a high carbohydrate diet. The disease is most frequent between the ages of 40 and 50 among Filipinos, Japanese and Chinese. Among Europeans it occurs most commonly between 50 and 70. The slight difference may be explained by the early maturity of Orientals as compared with Europeans. Diabetes mellitus as it occurs among Filipinos is of a milder type than among Europeans and Americans. The mortality is low and only a small percentage die of diabetic coma. The low incidence of diabetes mellitus among Filipinos and other Orientals may be explained as due either to greater power of assimilation for sugar among these people compared with Europeans and Americans, or to the fact that they are less exposed to continuous nervous strain on account of their peculiar modes of living. It may also be due to some peculiar racial tendency or characteristic.—R G H

(DIABETES) The influence of the phosphoric radical on blood and urine sugar in man (*Die Wirkung des Phosphorsäureions auf den Blut und Harnzucker des Menschen*) Elias (H) & Weiss (S), Wien Arch f innere Med, 1922, 4, 29-58

Intravenous injections of hypertonic solutions of NaH_2PO_4 or Na_2HPO_4 are generally followed by a decrease of the blood sugar when this quantity is high, as in diabetes or in alimentary hyperglycemia. The normal blood sugar content is not altered, however, after these injections. When the blood sugar is high and the urine contains sugar the injections decrease the sugar in the blood for 2-4 hours and in the urine for 3 days. This is true in all cases of diabetes, whether light or serious. It is possible that this is due to an influence of phosphates on the intermedial metabolism as well as on the kidneys. Other salts do not have this effect. The bisodium salt is about twice as active as the monosodium salt. The authors first believed that this action was perhaps due to a diminished quantity of phosphorus in the blood of diabetics, but they found this quantity of phosphorus to be within the normal limits. Then a second theory was formed, namely, that the sugar partly disappeared from the blood because dextrose diphosphoric acid was made by combination of the phosphoric acid and the glucose. This seemed possible, but its existence was never proved. No influence was seen on oxydative glycolysis by the injections. No explanation of this remarkable fact could be given. (See *Endocrin*, 1922, 6, 136).—J K

Acetone substances in the blood in DIABETES Fitz (R), Tr Ass Am Physicians, 1917, 32, 154-158

No quantitative relationship between increased concentration of acetone and lowering of blood bicarbonate was found, although in general the proportion of the acetone rose as that of the bicarbonate fell. The total acetone was increased by large amounts of fat, the maximum occurring several hours after ingestion and after visible lipaemia had disappeared. Small amounts of fat depressed blood-acetone. Fasting and pure carbohydrate diet diminished a high acetone value. NaHCO_3 increased the output of acetone, but its effect on blood-acetone was uncertain. In 3 fatal cases of coma, a rapid premortal rise of blood-acetone occurred, in one case this was independent of acidosis—Physiol Abst, 7, 121-122

(DIABETES) Familiar hemochromatosis (Über familiäre Haemochromatose) Frisch (A. V.), Wien Arch f innere Med, 1922, 4, 149-166

A case of bronze diabetes is reported. The patient showed a dirty brown color of trunk and limbs and a dark brownish color of face, neck, hands and skin of scrotum and penis. The skin of the abdomen, the back and the prepuce showed many very dark pigment marks. The patient died in a diabetic coma. A very extensive post-mortem report is given. Pineal and thyroid were normal, but the thyroid contained much pigment. There was cirrhosis of the liver, with an enormous quantity of pigment in the cells of Kupffer, in the connective tissue and in the epithelium of the bile ducts. The pancreas showed marked sclerosis with atrophy of the glandular parenchyma. Very few or no islands of Langerhans were found. Much pigment (hemosiderin) was found, partly intra-epithelially, partly interstitially, situated. The spleen contained little pigment, the follicles were atrophied, the trabeculae were partly degenerated. The connective tissue was increased. The lymph glands were very rich in pigment, in the retroperitoneal glands the lymphoid tissues had disappeared. The bone marrow was fat marrow with only a few spots of myeloid tissue, it did not contain much pigment. It was found in the mononuclear cells of the myeloid tissue, in the endothelium of the blood vessels and in the cells of the reticulum. The adrenals showed a normal structure, the cortex was poor in lipid and was hyperemic. The epithelium of the glomerular zone contained much hemosiderin. The hypophysis contained hemosiderin, especially in the eosinophil cells of the pars anterior. The pars nervosa, too, contained much pigment. The patient had 8 brothers and sisters, who, according to him, were also pigmented. The two brothers seen by the author were pigmented and had an indurative sclerosis of the liver, but no diabetes. Formerly there were many theories as to the relations between pigment and diabetes. It is now generally accepted that hemochromatosis is a predisposition to diabetes. That this theory is true is proved by this case in which two brothers do not have diabetes, but have all the other

symptoms of bronze diabetes The author believes that cirrhosis of the liver as well as diabetes is due to hemochromatosis He accepts the theory of Eppinger that in hemosiderosis the endothelium elements of the body have lost their power to change the iron into a substance that the other cells of the body want If this theory is true,—that bronze diabetes is a disease of the complete endothelial apparatus of the body,—it belongs to the same class as splenomegaly of Gaucher or hemolytic icterus There are two types of hemolytic icterus, the familial type (Minkowski) and the individual type (Hayem) These cases of hemochromatosis prove that here, too, not a congenital but a familial and an individual type exist —J K

DIABETES in negro Report of eight cases Goldstein (H I), New Jersey Med Soc J (Orange), 1922, 19, 157

Eight cases of diabetes in the negro are reported by Goldstein in a series of 65 cases of diabetes mellitus Apparently, diabetes in the negro is much less common than in the white population Syphilis is not an important causative factor in negro diabetics

—J Am M Ass, 1922, 79, 329

(DIABETES) Glycemia and glycosuria Graham (G), Lancet (Lond), 1921, 1, 1002-1007

This is the second of a series of three lectures by the author on this subject It deals primarily with the various conditions under which sugar is excreted in the urine Sugar may appear in the urine in other conditions than in diabetes mellitus, and other sugars than glucose frequently are found In such cases there is excretion of copper sulphate reducing substances without symptoms of diabetes No treatment is required for cases of diabetes innocus or renal diabetes The sugar tolerance test is employed to confirm the diagnosis of diabetes mellitus when sugar is found in the urine It is pointed out also that the "leak point" or kidney threshold is very low in non-diabetic cases of glycosuria, sugar often being found in the urine when the blood sugar is normal The author is of the opinion that the increased elevation of the renal threshold often found in diabetes is a defensive mechanism —I M

(DIABETES) Glycemia and glycosuria Graham (G), Lancet (Lond), 1921, 1, 1059-1065

This is the third of a series of three lectures on this subject The various hypotheses advanced to explain the cause of diabetes and the modern types of diabetic therapy are considered A brief but comprehensive discussion of the literature on the pathology of diabetes is included The author then describes experiments made by himself on two severe cases of diabetes in which he found sodium bicarbonate therapy to be of value because it increased the alkali reserve and because it caused increased elimination of acetoacetic

acid The latter substance the author, like Hurtley and Trevan, believes is the cause of coma in diabetes Neutral acetoacetates when given to animals intravenously in large doses cause symptoms of coma This indicates that it is not the added H-ions of the acetoacetic acid that cause diabetic coma and explains the failure of alkali therapy in this condition—I M

Functional tests in DIABETES Offenbacher (R) & Hahn (A), Arch f Verdaungskr (Berl), 1922, 29, 318

This communication from Strauss' service emphasizes that a single record of the blood gives no reliable information as to the normal or abnormal character of the carbohydrate metabolism This can be estimated with precision from the behavior of the sugar content of the blood during the first three hours or more after ingestion, fasting, of 50 gm of glucose in 300 cc of tea With true diabetes, the glycemia does not rise to its peak until the second or third hour, and sugar always appeared in the urine The details of nine cases of diabetes, free from glycosuria at the time, are tabulated From 0.125 the glycemia ran up to 3.36 in the second hour in one case, and the reaction was evident for three hours If the glycemia after the peak in the second hour returns promptly to normal, then the disturbances can be ascribed to neurasthenia or endocrine factors If it lasts longer than this, a true disturbance of the intermediate sugar metabolism seems certain

—J Am M Ass, 78, 1934

The acetonuria of DIABETES Hubbard (R S) & Nicholson (S T Jr), J Biol Chem (Balt), 1922, 53, 209-230

A method has been described for calculating a molecular ratio between ketogenic and antiketogenic compounds contained in the diet which is applicable to diabetic patients, and 7 cases have been described in which a comparison was made between the values of this ratio and the excretion of the acetone bodies in the urine It has been shown that the acetone excretion varies inversely with the numerical values of this ratio A study of the numerical values of the ratio calculated for the diets which correspond with a slightly increased excretion of acetone shows that they were approximately the same as those values found for normal subjects receiving diets low in carbohydrate, but containing sufficient calories to supply the needs of the subject It has been shown that fat fed sometimes increases the amount of acetone excreted, even when the increase replaces a part of the fat which the body was probably withdrawing from its own reserve supplies of this material—F S H

The chemistry of DIABETIC glucosuria Ionescu (A), Bull soc chim Rumania, 1921, 3, 97-104

A discussion of the chemistry of the diabetic organism chiefly of theoretical interest —Chem Abst, 10, 1620

Clinical aspect of studies on the metabolism of **DIABETES** Joslin (E P), Tr. Ass Am Physicians, May 2-4, 1922

Prior to the introduction of treatment by undernutrition, the average urinary nitrogen excreted per kilogram of body weight for 24 hours was 0.265 gm. After that time, for a considerably larger series of cases, the average urinary nitrogen excretion was 0.185 gm per kilogram of body weight for the 24 hours. The average metabolism for the early series was + 12 per cent and for the later series — 11 per cent. Comparison of the urinary nitrogen determinations with loss in body weight with metabolism and with the respiratory quotient suggest that protein metabolism alone does not control the total metabolism, that exogenous protein may be more stimulating to the metabolism than endogenous protein, that a very high nitrogen excretion in a severe diabetic may represent the prelethal rise, and that even such a diabetic may have the power to oxidize carbohydrate to a degree which is often not appreciated, but obviously should be utilized —J Am M Ass, 1922, 79, 71

The treatment of **DIABETES** by the general practitioner Joslin (E P), Penn M J (Harrisburg), 1922, 25, 373-381

A splendid concise summary of modern methods in treating diabetes mellitus, with an appeal to the country practitioner and city internist to familiarize themselves with these advances. The author's well known tables of food values and diabetic diets illustrate the article, which greatly help to simplify the arithmetic of modern diabetic dietetic therapy. Test diets, and maintenance diets are explained, the prevention of diabetes, causes of death in diabetes, treatment of diabetic acidosis, gangrene and infections, surgery in diabetes, indications and values of blood sugar determinations are all tersely reviewed —H L

Today's problem in **DIABETES** in light of nine hundred and thirty fatal cases Joslin (E P), J Am M Ass (Chicago), 1922, 78, 1506-1510

This is a statistical study of the progress in treating diabetes by Allen's method as compared with the years before the adoption of treatment by undernutrition. A brief exposition of the test and maintenance diets as used by the author is also presented. The article is not suited to more detailed abstraction —W M A

(**DIABETES**) The action of heterogenous proteins on the organism. Heterogenous proteins and glucose in the blood (*Recherches sur l'action des protéines hétérogènes dans l'organisme. Protéines hétérogènes et glycose dans le sang*) Lüttichau (A).

Arch internat de physiol (Liège & Par), 1922, 19, 1-15, abst ,
Physiol Abst , 1922, 7, 250

The intravenous injection of small quantities of certain proteins (ovoglobulin, but not ovalbumin, saliva, and casein) causes hyperglycemia, but not glycosuria in dogs, $\frac{1}{2}$ to $\frac{1}{3}$ of the proteins injected can pass out in the urine. Since the injection of the white of egg has a lymphagog, hepatic action, it is supposed that in the case of ovoglobulin there is also excitation, due to the formation of glucose in the liver, rather than a diminution in the consumption of the glucose. The author uses these experimental data in the discussion of the mechanism of glycosuria which is sometimes seen after the ingestion of proteins in persons with diabetes but not glycosuria.—R G H

Effects produced on DIABETES by extracts of pancreas Macleod (J J R), Banting (F G), Best (O H), Collip (J B), Campbell (W R), Fletcher (A A) & Noble (E C), Tr Ass Am Physicians, May 2-4, 1922

Researches on the action of pancreatic extracts have hitherto failed to take into account that there might be a powerful proteolytic enzyme which could destroy or digest any internal secretion also present. The authors have sought to obtain the pancreatic secretion isolated from such a proteolytic ferment, and to study its independent action. A highly potent product was obtained in small quantities from cattle fetus pancreas, which was termed "insulin." This is harmless to man and to laboratory animals when given in proper dosage, but toxic in large proportions. In 7 cases of human diabetes mellitus, subcutaneous injection of insulin reduced the blood sugar to normal level with disappearance of sugar and ketone bodies from the urine. The improved carbohydrate metabolism was evidenced by improvement in the respiratory quotient, which rose decidedly within two hours, while the patients felt a marked improvement in symptoms and in general well being. Laboratory experiments indicate that the pancreatic extract employed contained properties controlling carbohydrate and fat metabolism, yet its clinical results cannot be estimated. Probably the dietetic treatment will still be foremost, but the extract promises to be of value in tiding the patient over those crises which are frequently uncontrollable by other means.—J Am M Ass , 1922, 79, 71

(DIABETES) Organ stimulation by roentgen ray Petersen (W F) & Saelhof (C C), J Radiol (Omaha), 1922, 3, 135-138

Experiments were carried out by the authors upon depancreatized dogs and the general conclusions drawn were that with moderate doses of roentgen rays applied over areas containing pancreatic rests there may result an augmentation of sugar excretion, followed by evidence of pancreatic stimulation with increased

sugar tolerance lasting from three days to three weeks. If the dose was too large or if a cumulative effect was produced there resulted a lowering of the sugar tolerance. Conditions for this type of experiment are much more favorable in the dog than in the human diabetic subject, but even in clinical cases there is some evidence that a diabetic process may be influenced by direct radiation, though such treatment is not advised in diabetic coma at present unless all other means prove of no avail.—R G H

Syphilitic origin of DIABETES (L'origine syphilitique du diabète)

Pinard (M), Bull et mém Soc méd d hôp de Par, 1921, 45, 760-765

Pinard, investigating the history of 23 cases of diabetes, found that 10 showed evidence of old acquired syphilis and 5 of hereditary syphilis, of the remaining 8 no inquiry for syphilis had been made. He mentions cases in which sugar disappeared in the urine during treatment with salvarsan and reappeared afterwards. He also mentions that Warthin found syphilitic lesions in six cases of diabetes, although they were unsuspected during life. Pinard concludes that syphilis, acquired or hereditary, is an important cause of diabetes, which may be due to pancreatic, hepatic, hypophyseal, or bulbar lesions, and that syphilitic diabetes may be benefited by anti-syphilitic treatment. Other observers, however, find evidence of syphilis in a smaller percentage of cases of diabetes. Thus Rosenbloom, in 139 cases of diabetes mellitus, found a positive Wassermann reaction in about 12 per cent. Intensive treatment had no effect in increasing tolerance for carbohydrates. He concludes that in about 6 per cent the diabetes was syphilitic in origin, and in about 6 per cent independent of syphilis. He quotes other observers as having obtained similar percentages.—Med Sc, 1922, 6, 187-188

(DIABETES) The practical importance of the alimentary hyperglycemia curve (Über die praktische Bedeutung der alimentären Hyperglykämie-Kurve) Rosenberg (M), Klin Wchnschr (Berl), 1922, 1, 360-362

The relation between the sugar in the blood and in the urine is extremely complicated. Comparatively small doses of glucose cause glycosuria when they are not given by mouth but by the rectum, so that they need not pass the liver. The author gave 100 gm of glucose to healthy persons and constructed an average normal blood sugar curve. In diabetes the blood sugar rises higher than in normal persons and it may be much longer before the original blood sugar content is reached. This seems to be an excellent way to diagnose between very light cases of true and of renal diabetes. In Graves' disease the curve is sometimes quite normal, even in extremely serious cases. In other cases it closely resembles the curve in diabetes.—J K

(DIABETES) Blutzuckerstudien I Kritik der Blutzuckerbestimmungsmethoden Rosenberg (H), Arch f exper Path u Pharmacol (Berl), 1922, 92, 153-164

A critical account of previous studies on the blood sugar
—Physiol Abst, 7, 250

Blood pressure studies in 140 cases of DIABETES mellitus Rosenbloom (J), J Lab & Clin M (St Louis), 1922, 7, 392-399

One hundred and forty cases of diabetes mellitus studied by Rosenbloom showed that the blood pressure in uncomplicated diabetes is normal or slightly under normal. In every case in the series where there was present a high blood pressure it could be demonstrated that an existing nephritis, arteriosclerosis or aortitis was present. In this series 22 cases of diabetes were complicated by hypertension—a percentage of about 16. The presence or absence of sugar in the urine had no effect on the blood pressure. A high blood pressure in diabetes is due to a chronic nephritis, arteriosclerosis or a cardiac hypertrophy —R G H

The chemical procedures that are of use in the control of DIABETES Snowden (R R), Penn M J (Harrisburg), 1922, 25, 383-389

The author considers the glucose content of the blood indispensable in the diagnosis and study of a diabetic. It is always above normal in a diabetic who is excreting sugar in the urine and not infrequently is above normal even when the urine is sugar free. Treatment, therefore, should be based on the blood sugar rather than the urinary tests. An accurate measure of the degree of acidosis can be obtained by measuring the alkaline reserve, and sometimes approaching acidosis can be detected before this is evident from the clinical picture —H L

(DIABETES) Sugar metabolism in man (Studien über den Zuckerstoffwechsel des Menschen) II & III Staub (H), Ztschr f klin Med (Berl), 1922, 93, 89-123, 123-140, Klin Wchnschr (Berl), 1922, 6, 1332

It is found that after a meal followed 10-15 hours later by the administration of 20 gm of glucose dissolved in 100 cc of water there is little rise of the blood sugar. When the time between the meal and the administration of glucose is more or less than 10-15 hours, there is greater increase of blood sugar. Staub was able to prove that a comparatively small rise of blood sugar and a short duration of this hyperglycemia after the ingestion of 20 gm of glucose was a sign of good carbohydrate assimilation, while long duration and high hyperglycemia are found when this assimilation is defective. Thus it may be concluded that assimilation of carbohydrates reaches its minimum after 10-15 hours of starvation. The changes in carbohydrate metabolism during starvation are probably

due to changes in the formation of enzymes which act upon the intermedial sugar metabolism. The formation of these enzymes depends both upon the quantity of carbohydrate in the body and those taken by mouth. When glucose is given during strenuous work the hyperglycemia is much less intense than when the person is at rest. After ingestion of glucose during work the hyperglycemia becomes hypoglycemia at the moment at which the person at rest has a maximum hyperglycemia. In a person with a normal dose of glycogen in his body the influence of glucose on the blood sugar during moderate work is the same as during rest, moderate work has the same influence on a person with a small quantity of glycogen as strenuous work has on a normal organism. When a person takes only fat and proteins for two days the rise of blood sugar after the ingestion of glucose is higher than when he has taken carbohydrates for two days.—J K

Causes of DIABETES (*Feststellungen zur Diabetesetiologie*)
Strauss (H), *Klin Wchnschr* (Berl), 1922, 1, 885-887

From the beginning of the war until the autumn of 1916, 1524 cases of diabetes were seen in the German army. In 70 cases the disease was caused by trauma, in 45 cases diabetes was seen after infection, 10 cases probably were due to shock. Of the other cases no details are known. Of these 1524 cases, 909 or 72.8% became diabetic during the war. Among the 70 traumatic cases, there were only 5 wounds of the skull. Among the infectious cases (45), 17 were due to dysentery, 4 to enteritis, 4 to typhoid fever, 3 to cholera and 2 to paratyphus. Enteric infections seem to play an important rôle.—J K

(DIABETES) A comparison of several clinical quantitative blood sugar methods. Thalheimer (W) & Updegraff (Helen), *J Am M Ass* (Chicago), 1922, 78, 1383-1388

The Benedict, the Myers and Bailey modifications of the original Lewis and Benedict method, and the latest modification of the Folin and Wu method for blood sugar determination are compared as to normal values and as to accuracy. The normal values are distinctly different by the three methods, so that it is necessary to report the method when giving a blood sugar estimation.—W M A

Postoperative pancreatic DIABETES Umber, *Klin Wchnschr* (Berl), 1922, 1, 1232

One-half year after an operation for a cyst of the pancreas the patient developed diabetes. Details are not given.—J K

Estimation of sugar in DIABETIC blood Vigevali (G), *Boll Chim Farm*, 1919, 58, 436-439

Two cc of the blood are mixed with 100 cc of KCl solution (saturate KCl solution 340 cc, HClO 375 cc, and water 160 cc),

50 cc of the mixture are boiled for 5 minutes, filtered from the precipitated proteins, the filtrate is made up to a definite volume, and 10 cc are introduced into an Erlenmeyer flask, around the neck of which rubber tubing has been fixed. From 1 to 2 cc (according to the amount of dextrose) of a Cu solution (Cu SO_4 22, KHCO_3 80, K CO_3 50, KCl 53 g, water, 500 cc) are added, the mixture is boiled for 3 minutes, and the rubber tube closed with a clip, so that after cooling a vacuum is produced within the flask. A current of CO_2 is then introduced and the liquid titrated with I solution (0.1 NHCl 5 cc, I 0.0635 g, KI 2 g, 2% KIO_3 solution 2 cc, and water to 100 cc) with starch solution 2 g soluble starch in 100 g of saturated KCl solution as indicator. The Cu reduced by the dextrose reacts with the I solution. The latter is previously standardized on pure dextrose which has been dried at 100° —Chem Abst, 16, 1260

(DIABETES mellitus) The ophthalmologists' standpoint Weissner (E A), Penn M J (Harrisburg), 1922, 25, 381-383

With the exception of diabetic cataract, eye symptoms in diabetes are more frequent, according to Weissner, where this disease is of long duration, and when it occurs mostly late in life, between 50 and 70 years of age. Diabetic cataracts affect both sexes equally, are usually binocular, very rapid in growth and soft in character. The treatment is operative just as in senile cataract. The dangers are slow healing, inviting infection, iritis and hemorrhage, followed by secondary glaucoma. Diabetic retinitis occurs late in the disease, is usually accompanied by some loss of visual acuity and changes in the vitreous with little hope of regaining any of the vision lost. Diminution in the range of accommodation, probably from some toxic action of glucose, is usually relieved by the elimination of sugar. Changes in refraction occur, usually myopia, and often cured by dietetic treatment. Diabetic amblyopia occurs occasionally and vision slowly improves under proper dietetic treatment. Extra-ocular paralyses may be due to diabetes, especially diplopia and ptosis—H L

Optimal food mixtures for DIABETIC patients Wilder (R M), J Am M Ass (Chicago), 1922, 78, 1878-1884

A satisfactory dietary should embody four principles (1) total dietary restriction, (2) protein restriction, (3) carbohydrate restriction, (4) balanced fat and carbohydrate. These principles are discussed and charts and formulas are given for calculating the optimal diet—W M A

(DIABETES) The threshold of ketogenesis Wilder (R M) & Winter (M D), J Biol Chem (Balt), 1922, 52, 393-401

Another paper built on assumptions which are employed in the calculation of the composition of the mixture of food substances

engaging in metabolism Under the conditions of the experiments reported here on man, providing the assumptions are tenable, the ratio between the ketogenic and the glucose molecule at which a clinically significant ketosis appears has a value of at least 2:1. A ratio of this value implies that every molecule of glucose is ketolytic for 2 molecules of acetoacetic acid. The existence of infection lowers the ketogenic threshold so that significant ketogenesis may occur with lower ratios. Other factors, thus far undetermined, may also lower this threshold. It is advisable, therefore, in planning diets for diabetic patients to allow only such food mixtures as will avoid the 2:1 ratio by a safe margin.—F S H

Objects and method of diet adjustment in DIABETES Woodyatt (R T), Arch Int Med (Chicago), 1921, 28, 125-141

Woodyatt reconciles and explains the confusion from such conflicting diets as the Falta "cereal cure," Donkin "milk cure," von Duering "rice cure," Mossé "potato cure," von Noorden "oatmeal cure," and recent low protein high fat diets of Newburgh and Marsh. He takes exception to the universal necessity or wisdom of the "total dietary restriction" and "undernutrition" regimes of Allen and Joslin. He points out that the quantity of oxidizing glucose fixes an upper limit to the quantity of ketogenic fatty acid that can be completely oxidized at the same time. The ratio of higher fatty acids to glucose, which if exceeded will lead to acidosis, is likely to be close to 1.5 to 1 (in gm). In diets below maintenance, the body tissues will be burned, and if the patient is fat, he will burn fat and but little protein, but if he has but little fat, he will utilize considerable body protein which means 58 glucose. This will hold down the amount of glucose that can be given in the diet as carbohydrate and protein. But if sufficient fat is given in the diet to prevent catabolizing of body protein, more glucose can be given in the diet—a higher caloric intake obtained and a better state of nutrition result. These principles are worked out mathematically and equations and ratios given. A practical example is included of a case in which these principles and methods were followed out systematically with most interesting and satisfying results.—H L

Confusion of methanol poisoning with DIABETES Zeigler, Brit J Ophthalmology, Am J Public Health, 1921, 11, 1115

It is noted that the end product excreted by the kidneys is formic acid and that this reduces Fehling solution so that a wrong diagnosis is possible.—Chem Abst, 16, 1278

Experimental DIABETES INSIPIDUS Bailey (P) & Bremer (F), Arch Int Med (Chicago), 1921, 28, 773-803

In order to throw further light on the pathogenesis of diabetes insipidus, systematic punctures of the hypothalamus were made in 23 adult dogs, employing the lateral route of Paulesco and Cushing.

giving perfect exposure, and avoiding any injury of the hypophysis. It was found that a lesion, even extremely minute, of the parainfundibular region of the hypothalamus provokes with certitude polyuria, which appears in the first two days and, according to the extent of the lesion, is transient or permanent. In the latter case cachexia "hypophyseopriva," genital atrophy and adiposity are present. Permanent polyuria has all the characteristics of diabetes insipidus in man, e. g., possibility of concentration when intake of fluids is restricted, when pituitary extract is injected subcutaneously, or in the presence of fever. Thirst may precede polyuria. Experimental diabetes insipidus does not depend on a disturbance of a supposed nervous or vascular regulation of the kidney, proven by its production in animals whose kidneys have been denervated. Lesion of the tuber cinereum produced in two dogs a cachexia "hypophyseopriva" with acute genital atrophy and in two other dogs an insidiously developing adiposogenital dystrophy. The integrity of the pituitary was in each case verified histologically. The same dogs had persistent polyuria —H L

Considérations sur la pathogénie du diabète insipide et du syndrome adipo-génital Bremer, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 605

See Endocrin, 5, 761-762 —R G H

DIABETE insipide syphilitique avec hémianopsie bitemporale et crises de narcolepsie Foix, Alajouanine & Dauplain, III Réunion neurol internat ann, Par, 1922, abst, Presse méd (Par), 1922, 30, 615

The authors report a case of infundibular syndrome analogous to that described by Claude and Lhermitte in a case of tumor of the third ventricle. The diabetes insipidus persisted in spite of antisiphilitic treatment —R G H

Renal GLYCOSURIA Marsh (P L), Arch Int Med (Chicago), 1921, 28, 54-61

A case of renal glycosuria is described. During a period of four months the patient excreted an average of 60 gm glucose daily with a variation of from 15 to 122 gm. The amount was not related to the carbohydrate intake. Diuresis by increased water ingestion caused no increase in the glycosuria, and no effect was seen from the administration of diuretin in large doses. No evidence of nephritis was found. The blood sugar curve was normal —H L

DIABETES INSIPIDUS Mikus, Klin Wehnschr (Berl), 1922, 1 1131

Demonstration of a patient with syphilitic diabetes insipidus and changes in the bones of the sella. Antisiphilitic treatment diminished polyuria and polydypsia, though the specific gravity of the

urine remained very low In the last months, however, the patient began to show symptoms of osteomalacia —J K

Metabolic studies on a case of DIABETES INSIPIDUS Rabinowitch (I M), Arch Int Med (Chicago), 1921, 28, 355-366

A man, aged 47, was carefully studied in the Montreal General Hospital, his was the only case of diabetes insipidus in the last 50,000 admissions The blood chemistry was as follows

Non-protein nitrogen	28 0	mg per 100 cc ,
Urea nitrogen	16 0	mg per 100 cc ,
Uric acid	1 1	mg per 100 cc ,
Creatinin	1 2	mg per 100 cc ,
Cholesterol	0 126	mg per 100 cc ,
Sugar	0 100	per cent,
Chlorids (as sodium chlorid)	0 627	per cent (plasma),
Total protein	7 4	per cent,
Albumin	4 6	per cent,
Globulin	2 8	per cent

The only abnormal finding was the hyperchloremia Basal metabolism estimation showed a normal rate The Goetsch test and Csepal conjunctival test were negative, suggesting hypofunction of the suprarenals The Ascoli subepidermal test was only slightly positive There was diminished sugar tolerance, suggesting hyperpituitarism The Mosenthal renal test meal showed faulty metabolism of salt and water The kidneys were unable to excrete chlorids properly Rabinowitch concludes that in his case no single specific lesion was found to account for the polyuria An endocrine and a renal factor were present Pituitary extract improved not only the concentration, but also the rate of excretion, suggesting that diabetes insipidus is caused by a lack of some internal secretion which normally regulates and moderates diuresis by acting on the renal cells —H L

A case of DIABETES INSIPIDUS with consideration on the mode of action of extract of the posterior lobe of the HYPOPHYSIS (Un cas de diabète insipide avec considérations sur le mode d'action de l'extrait de lobe postérieur d'hypophyse) Souques, Alajouanine & Lermoyez (J), III Réunion neurol internat ann , Paris, 1922, abst , Presse méd (Par), 1922, 30, 615

A case is described of a young girl with diabetes insipidus of unknown etiology and with polyuria of 16 litres The renal function was normal The influence of extracts of the posterior lobe of the hypophysis was remarkable, but lasted only 8-10 hours A series of experiments to decide the mode of action of these extracts did not determine whether the pars intermedia or the pars nervosa played the principal rôle Renal polyuria was affected and even in normal subjects the action was that of a medicament rather than of organo-therapy —R G H

DIABETES INSIPIDUS Umber, Klin Wchnschr (Berl), 1922, 1, 1232

A short note The patient had hemianopsia and polyuria The skiagram showed no changes in the sella As the Wassermann test was positive, antisyphilitic treatment was given The patient is completely cured —J K

(ENDOCRINE ORGANS) Further studies on substances with specific action prepared from single organs VII Chemotactic experiments on *Paramecia* and experiments on the velocity of their division under the influence of optones from different organs (Weitere Untersuchungen über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung VII Chemotaktische Versuche an *Paramecien* und Untersuchungen über die Geschwindigkeit ihrer Teilung unter dem Einfluss von Optonen aus verschiedenen Organen) Abderhalden (E) & Schiffmann (Olga), Arch f d ges Physiol (Berl), 1922, 194, 206-217

Optones from the corpus luteum, pituitary, ovary, thyroid and thymus, diluted 1:100 act fatally, or negatively chemotactic on *paramecia*, still greater dilutions show positive chemotaxis Specific actions of single optones cannot be observed Optones from thymus, testis, and thyroid increase the intensity of division, while those from pituitary and corpus luteum retard it The retardation from pituitary is overcome by repeated treatment —A T C

Action of extracts of the ENDOCRINE GLANDS upon the isolated uterus, particularly after castration (Action d'extraits et produits dérivés d'organes à sécrétion interne sur l'utérus isolé, particulièrement après la castration totale) Athias (M), Arch internat de pharmacad et de therap (Gand & Par), 1921, 25, 423-452

A confirmation of the results of previous workers on the response of the isolated uterus of different species to extracts of the pituitary and suprarenal glands Rhythmic contractions disappear after castration, but otherwise the behavior is normal after this operation A reversal of the adrenalin effect after pituitary was not obtained —Physiol Abst, 6, 327

(ENDOCRINE) The calcium content of the blood in guanidine poisoning (Über den Calciumgehalt des Blutes bei der Guanidinvergiftung) Bayer (G), Ztschr f d ges exper Med (Berl) 1922, 27, 119-126

Guanidine poisoning causes in rabbits, cats, and guinea pigs in a few hours a decrease of the Ca ions in the blood This decrease is usually smaller than after the extirpation of the parathyroids, but it may be as high —Physiol Abst, 1922, 7, 257

(ENDOCRINE) Pathogenesis of congenital *fragilitas ossium* [Beitrag zur Kenntnis der Pathogenese der *Fragilitas ossium congenita* (Osteopasthyrosis infantilis)] Bolten (G C), Deutsche Ztschr f Nerven (Leipz), 1919, 63, 343-359

Reports of three cases of *fragilitas ossium* Two patients were brothers, aged 18 and 11 years respectively, the third was a 3 year old girl All were from neuropathic families, and showed blue sclerae, very fragile bones and various vasomotor-trophic disturbances, for example, frequent attacks of urticaria, cold, clammy hands and feet, etc Bolten believes that this condition is the result of disturbances in the trophic function, and that this has its cause in a hypotonia of the vegetative (especially of the sympathetic) nervous system and of the therewith functionally inseparable "accelerating glands of internal secretion" In addition to the above clinical observations, Bolten thinks that his view is supported by two arguments, namely, (1) that there were very many manifestations of sympathetic hypotonia present not only in the three patients, but also in the mother and other brothers and sisters of the first two patients, and (2) that in the family of the third patient there was a remarkably large number of cretins and also manifestations of vagotonia —J P S

(ENDOCRINE) Vasomotor neurosis cured (Die vasomotorische Neurose Nothnagels) Bolten (G C), Deutsche Ztschr f Nerven (Leipz), 1921, 70, 256-265

This is a report of a case in a woman 52 years old The condition was characterized by paresthesias, pains, especially burning pain, in different parts of the body, sensory disturbances, hyper- and hypo-esthesias, and vasomotor disturbances Such cases usually occur in females about the time of the menopause Bolten, therefore, thinks that failure of the internal secretion of the ovaries plus disturbances of the adrenal lead to hypotonia (vagotonia) This patient improved on small doses of ovarian, thyroid and adrenal preparations When the patient stopped the medication for a time the paresthesias returned, to disappear again on resuming the treatment —J P S

(ENDOCRINE ORGANS) Neurological metabolism of the medulla oblongata II Experiments on the regulation of the carbohydrate metabolism in the oblongata (Zur Stoffwechselneurologie der Medulla oblongata II Experimenteller Beitrag zur Regulation des Zuckersstoffwechsels in der Oblongata) Brugsch (T), Dresel (K) & Lewy (F H), Ztschr f d ges exper Med (Berl), 1921, 25, 262

It was previously shown that the pigûre point in the 4th ventricle is identical with the sympathetic-vagus nucleus Stimulation thereof did not always induce hyperglycemia Examination of serial

sections of the place of injury now shows that when the posterior 3rd was touched hyperglycemia resulted. When the anterior half was stimulated a hypoglycemia ensued. The anterior half sets the suprarenals in action, the posterior portion controls the vagus fibres to the pancreas — *Physiol Abst*, 7, 97

(ENDOCRINE) Roentgenological findings in Mongolism. Clift (M W), *Am J Roentgenol (N Y)*, 1922, 9, 420-422

The author takes issue with Timme, who has reported a characteristic sella turcica picture in Mongolism. In Clift's opinion there is no single characteristic roentgenological sign in this disease, and the only departure from normal is a generalized delay of bone development. This feature, except for a slight selective character on the part of the nose and maxilla, is common to a number of other diseases, some of endocrine origin and others due to obscure causes

—R G H

(ENDOCRINE) Insuffisance pluriglandulaire fruste et troubles mentaux chez un hérédo-syphilitique avec rhumatismes chroniques ankylosants post-infectieux. Cornil & Robin (G), *Soc clin de méd mentale*, May 15, 1922, abst, *Presse méd (Par)*, 1922, 30, 481

The authors describe a hereditary syphilitic who had, at 9 years, a meningeal infection, complicated by cervical spondylosis, ankylosis of the hips and radiocubital synostosis, and recently by epilepsy and mental disorders. Due to the insufficiency of the thyroid, testicle and hypophysis, the authors believe these troubles to be caused in most cases by hereditary syphilis, though there is the possibility of pluriglandular insufficiency from general infection

—R G H

Glandular adipose tissue and its relation to other ENDOCRINE ORGANS and to the vitamine problem. Cramer (W), *Brit J Exper Path (Lond)*, 1920, 1, 184-196

As a result of experimental work, mostly on white rats and tame mice, but also with the perinephric fat of the guinea pig, rabbit and man, the author concludes that in all these forms there exists a glandular type of adipose tissue (variously known as "brown fat," "hibernating gland," etc), which is histogenetically and functionally distinct from ordinary adipose tissue, although in most species it acquires the appearance of ordinary adipose tissue soon after birth. Stress is laid upon the fact that the fatty material of this glandular adipose tissue is rich in cholesterolin compounds and other lipoids in addition to true fat, and that these lipoids are largely retained during ordinary starvation but are used up in animals dying from having been on a vitamine-free diet. With this loss of lipoid, the tissue comes to resemble a very vascular endocrine organ. Possibly the lipoid has been used up to supply vitamines. Since vitamine deficiency also causes great loss of lipoid from the suprarenal cortex

and since there is great similarity in the reaction to polarized light between the adrenal cortex and this glandular adipose tissue, the author assumes that there is also great similarity in composition between these two tissues. The glandular adipose tissue may also be closely related to the function of the thyroid since the fatty accumulations in cretins have by some been considered enlargements of this glandular type of adipose tissue. The conclusion is that disturbances of the functional activity of this glandular adipose tissue will have to be taken into consideration in connection with deficiency diseases. "Lipoid gland" or "cholesterin gland" is suggested as a better name for this tissue —A T R

(ENDOCRINE) Sterility Forsdike (S), Practitioner (Lond), 1922, 108, 243-251

Sterility in the female may be due to persistence of undeveloped organs, altered secretions of the genital tract (infectious), gross lesions of the tract (tumors or trauma), functional causes, vaginismus, metabolic changes or changes of the internal secretions, or failure of ovulation. Nothing further of endocrine interest is included —H L

The ENDOCRINE system some relations to ophthalmology and otolaryngology Fridenberg (P), Penn M J (Harrisburg), 1922, 25, 523-527

The profound influence of the ductless glands upon the structural development and function of the entire body obviously suggests a relationship oftentimes to anomalies of development and derangements of function in the domain of ophthalmology and otolaryngology. The author suggests that hyperthyroidism may lead either to exophthalmos or glaucoma, depending on whether the eye structure is vagotonic in type. The latter is characterized by a stiff sclera, large lens, small pupil, ripe for an acute attack of glaucoma if there is an excessive sympathicotonia as in hyperthyroidism. Fridenberg distinguishes two endocrine ocular types. The pituitary eye is recessed, enophthalmic, with small lid fissure, contracted pupil and tendency to marked pigmentation and hyperopic refraction. The hyperthyroidic eye shows exophthalmos, mydriasis, large lid fissure, vascularity of conjunctiva and lids, and a tendency to epiphora, subnormal accommodation, defective convergence and the various asthenopias —H L

ENDOCRINE glands and their importance in tropical pathology (Nociones sobre las glandulas endocrinas y su importancia in la patologia tropical) García de Quevedo (L), Bull Porto Rico Med Ass, 1922, 16, 65-73

A general summarizing discussion of present day endocrinology, not amenable to abstracting —R G H

(ENDOCRINE ORGANS) Dwarfism and gigantism (Über Zwergwuchs und Riesenwuchs mit einem Beitrag zum Studium verwandter Entwicklungstörungen im Organismus) Gigon (A), Schweiz Arch f Neurol u Psychiat (Zürich), 1921 9, 283-302, 1922, 10, 113-129

This article includes the history, physical findings, x-ray findings, etc, in 10 cases of abnormally small or unusually large patients with a discussion of their classification and the involvement of the ductless glands, with the conclusion that there is great need for new clinical investigations on such morphological characters as skeletal form, adiposity, mammary glands, hirsute, etc. Ninety-eight references are given.—A T R

(ENDOCRINE ORGANS) The influence of the nervous system on adipose tissue (Über den Einfluss des Nervensystems auf das Fettgewebe) Goering (Dora), Ztschr f Konstit (Berl), 1922, 8, 312-335

This is incidentally of endocrine interest since the influence of the glands of internal secretion (particularly the thyroids, gonads, hypophysis and epiphysis) on adipose tissue is discussed because it is a question whether this influence is direct or indirect through the nervous system. There is a review of the evidence for the existence of various vegetative centers, especially in the region of the floor of the third ventricle, which might influence fat metabolism. From a study of lipodystrophia progressiva, lipomatosis, adipositas, dolorosa, scleroderma, glossy skin, hemiatrophia and hemihypertrophia faciei the author concludes that various nerve centers and the sympathetic nervous system are intimately involved. In connection with clinical and experimental dystrophia adiposo-genitalis the conclusion is drawn that the fat regulating center is in the floor of the third ventricle. It is mostly based upon literature, 126 references being given.—A T R

(ENDOCRINE) The new clinic. An advance movement in child welfare and race regeneration. Haberman (J V), Boston M & S J, 1920, 182, 450-451

The author points out, among other things, the desirability of a careful survey of the endocrine status of each child, with a view to early corrective procedures in case of defects.—R G H

(ENDOCRINE) Sclérodémie partielle traitée avec succès par l'opothérapie associée. Hügel, Cong d Dermatol et Syphil de langue franç, 1922, abst, Presse méd (Par), 1922 30, 561

A woman of 25 years was troubled with scleroderma in the foot and calf of leg which inconvenienced her considerably in walking and in her work. All other treatment having failed, the author prescribed extracts of thyroid, ovary, hypophysis and adrenal. In 15

days the lesions had almost disappeared and no longer interfered with her work. The author believes that in Alsace scleroderma is about equally frequent with goiter—R G H

(ENDOCRINE) Organotherapy in nervous conditions (*Innersekretorische Therapie bei nervösen Zuständen*) Laubenheimer, Klin Wchnschr (Berl), 1922, 1, 1329

A short note. Thyroid is recommended for migraine. Hypophysis proved to be beneficial only once. Parathyroid and ovary are useless—J K

Epileptiform manifestations in ENDOCRINOUS disorders Leahy (S R), N York State J M (N Y), 1922, 22, 8-14

There appeared to be a definite relation between deficient ovarian secretion and epileptiform attacks. There appeared to be a definite relation between *dyspituitarism* attended by deficient secretion and epileptiform attacks. Practically all of the cases showed more than one glandular involvement. Striking physical abnormality was absent, except in one case. The failure of the attack to disappear entirely in some cases may be due to the effect that glandular involvements other than those established were overlooked, and therefore not medicated, or establishment of the epileptic habits rendered this form of discharge of energy more difficult to control after being present for some time. Transitional forms of various endocrinous disturbances should be sought for in every case of epilepsy—Arch Diagn, 1922, 14, 257-258

Le syndrome ENDOCRINO-sympathique de la pelade (alopecia) Lévy-Frankel & Juster, Cong d Dermatol et Syphil de langue franç, 1922, abst, Presse méd (Par), 1922, 30, 561

Along with alopecia the authors always find endocrine disorders—*dysthyroidism*, *dysovarianism*, *frigidity*, *hypophysis* disorders, modifications of the oculo-cardiac, pilomotor and nasofacial reflexes, vasomotor troubles (*dermographia*, frailty of skin). These troubles and alopecia are favorably modified by organotherapy. The authors conclude that alopecia is due indirectly to the endocrine system—R G H

(ENDOCRINE) Syphilis C F M & C L, Med Sc (Lond), 1921 3, 229-301

The article includes an excellent brief review of the current data on syphilis of the endocrine glands—R G H

(ENDOCRINOLOGY) The oculo-cardiac reflex (*Dagnini-Aschner phenomenon*)—its use in medicine and psychology Naccarati (S), Arch Neurol & Psychiat, 1921, 3, 40-57, abst, Med Sc (Lond), 1921, 4, 150-151

Naccaratì gives a list of factors, both physiological and psychological, which influence the character of the response in normal subjects, and it becomes clear from his observations that the oculo-cardiac reflex has no diagnostic value whatever. It is unfortunate that he does not say this at once, and thus put in its proper perspective a phenomenon which has cumbered neurological literature unduly. Instead, he goes on to say that "it may constitute an index of the psychic condition and of the sympathetic-endocrine make-up of the subject, but only when other factors have been standardized. In normal persons the reflex index may serve as an indication of reflex control, moods, courage, emotions, etc., traits whose scales are wanting." All of which means precisely nothing. It seems characteristic of the craving for new and bizarre "signs," for ever fresh empirical diagnostic tricks, that it gives rise to an extensive and unscientific literature, which rises mushroom-like as each new phenomenon is recorded. The quotation given above from Naccaratì's paper is typical of the scientific value and general style of the papers in which these new signs and wonders are proclaimed. The atrocious phrase "sympathetic-endocrine make-up" is an epitome of this class of neurological literature.—Abbreviated, R G H

Referat uber INNERE SEKRETION Nakamura (H), Verhandl d jap path Gesellsch (Tokyo), 1916, 6, Reprint 1-9

An outline classification of endocrine disorders, illustrated with two excellent plates—R G H

(**ENDOCRINE**) New method of sterilization of organo-therapeutic products (*Un nuovo metodo di sterilizzazione dei prodotti organo-terapici*) Paranhos (P), Ann d'ig (Roma), 1921, 31, 620

By means of an isotonic solution of sodium fluoride, organo-therapeutic products can be obtained containing 0.10 gm of the given organ and 1 mgm of NaF to every cc of the final product. Preparations of this sort remain indefinitely sterile and do not give rise to any trouble when injected into man.—Med Sc, 1922, 6, 233

Histological changes in the ENDOCRINE organs after injections of ADRENIN and choline (*Studi sul timo II Glandole endocrine e sangue nei polli iniettati con adrenalina e con collina*) Pighini (G), Riv sper di freniat (Reggio-Emilia), 1921, 45, 1-40

Investigations of the histological changes occurring in various endocrine organs as the result of injections of adrenaline and choline. In the thymus adrenaline produced degenerative and choline hypotrophic effects.—Physiol Abst, 7, 257

(**ENDOCRINE**) physiopathology of "vicious circle" after gastro-enterostomy and its relation to high obstruction (*La fisiopatologia del "circolo vizioso acuto" consecutivo alla gastroenterostomia*

nei suoi rapporti colla occlusione alta) Razzaboni (G), Arch ital di chir, 1921, 4, 553, abst, Med Sc, 1922, 6, 201

Intestinal occlusion was performed in dogs The adrenals and thyroid showed evidence of toxic degeneration —R G H

Influence of the ENDOCRINE organs on morphogenesis (Weitere Untersuchungen über die Wirkung innersekretorischer Drusensubstanzen auf die Morphogenese) Schulze (W), Klin Wchnschr (Berl), 1922, 1, 895-896

The author tried to remove completely the thyroid "anlagen" in 25 tadpoles of *Rana fusca* He succeeded in only 6 animals, 4 of these were lost, the only two that were left grew rapidly, but metamorphosis began only when bovine thyroid was given One tadpole without "thyroid-anlage" to which no thyroid was given has been living for over a year as a tadpole In another series of experiments the author implanted in larvae of *Bombinator pachypus* thyroid of *Bombinator pachypus*, thyroid of the cow, normal human thyroid, thyroid of Graves' disease and testicles The implantation of testicle had no effect The implantation of thyroid caused a quickened metamorphosis with an arrest of growth The influence of human and bovine thyroid was much more marked than was the thyroid of the same species In some of the animals metamorphosis was so fast that they died In one case, real prolapse of the brain was seen, this proves the great importance of endocrine secretions in the genesis of malformations —J K

(ENDOCRINE) *Maladie de Recklinghausen avec insuffisance polyglandulaire* Røederer (J), Réunion Dermatol de Strasbourg, May 14, 1922, abst, Presse méd (Par), 1922, 30, 507

A typical case is described of neuro- and dermo-fibromatosis with pigmentary lesions in a young girl of 19 years, whose mother also has pigmentary trouble There is a hypoplastic thyroid, acroasphyxia and little resistance to fatigue The author believes that endocrine factors play a more or less important rôle in the pathogenesis of this disease and proposes the use of extracts of thyroid, ovary and hypophysis in treatment —R G H

(ENDOCRINE) *Syndrome polyglandulaire à symptomatologie complexe* Sainton & Peron (N), III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 615

A man of 25 years, after having had meningitis at 10 months, continued to have optic atrophy and nystagmus The patient showed adiposity, pseudogynecomastia, genital hyperplasia, and frigidity He was tall in spite of marked kyphoscoliosis The sinus was enormous, but the sella turcica was normal There was also considerable thyromegaly and tremor The biological hypophyseal tests were negative This case brings up the question of the relation between

meningitic lesions of the base of the brain and the appearance of different symptoms of so-called hypophyseal syndromes—R G H

(ENDOCRINE) An analysis of ninety cases of functional disease in soldiers Swan (J M), Arch Int Med (Chicago), 1921, 28, 586-602

The ages, occupations, previous histories, particular complaints, symptomatology, pulse studies after exercise, blood pressures, etc., are all carefully recorded and tabulated. These are the cases variously diagnosed as irritable heart, effort syndrome, neurocirculatory asthenia, etc. Sixty-five per cent were recruited from sedentary occupations, 50 per cent gave a family history of nervous disease, no evidence of organic disease to explain the symptoms complained of could be found in any of them, 90 per cent gave evidence of previous or present subacute chronic infections. Some evidence of ductless gland disturbance was found in all of them. Removal of the foci of infection did not benefit the patients. Swan is strongly of the opinion that endocrine abnormality is the responsible factor. The treatment is very largely psychic. Organotherapy is not advised.—H L

(ENDOCRINE) Clinical interpretations of the basal metabolism test Swanberg (H), Illinois M J , 1922, 42, 39-41

Attention is called to the importance of the correct interpretation of basal metabolism findings. Basal metabolism is increased in thyroid and pituitary hyperactivity, the leukemias, the fevers, late pregnancy, pernicious anemia, early diabetes, and cardiac decompensation. Basal metabolism is decreased in thyroid and pituitary hypoactivity, Addison's disease, extreme cachexia from tuberculosis, diabetes, starvation, and in some healthy persons running a slow pulse. A combination in a patient of two or more conditions characterized by opposing basal metabolism findings may in totality yield a plus or minus rate depending upon which disease plays the leading rôle in the patient. While in non-endocrine conditions (leukemia, diabetes, etc.) diagnosis can readily be made without basal metabolism observations, this laboratory procedure has become a necessity in diagnosis of diseases involving the thyroid and pituitary glands. Moreover, basal metabolism findings determine the severity of thyroid malfunction and indicate the treatment required.—I B

The etiological relation of the eye to the ENDOCRINE organs Zentmayer (W), Penn M J (Harrisburg), 1922, 25, 527-529

Extirpation of the thyroid in dogs leads sometimes to porcelain-white corneal infiltration, blepharitis, lacrimation, conjunctivitis and partial blindness. Interstitial keratitis and bilateral cataract have followed complete excision of the thyroid and parathyroids. The ocular complications of disease of the pituitary are regarded as produced by direct pressure and increased intracranial pressure.

However, glandular therapy has relieved amblyopia in undoubted hypophyseal disease. The ocular symptoms of hyperthyroidism, though very striking, are not constant and bear no relation to the gravity of the toxemia. The eye changes observed in myxedema, cretinism and mongolian idiocy are briefly mentioned. The possible bearing of endocrine disease on pigmentary degeneration of the retina and amaurotic family idiocy is commented upon —H L

(GONADS) Experimental hyperfeminism (Ueber experimentellen Hyperfeminismus) Bondi (J) & Neurath (R), Wien klin Wchnschr, 1922, 35, 520-522

It is probable that the endocrine products of the mother during pregnancy have an influence on the child. This explains the fact that during the first days after birth the mammary glands of the child function slightly and that many new born girls bleed from the generative organs. To study this question experimentally the authors transplanted the ovaries of young rats in other female rats of the same age. The first remarkable effect was that out of 27 animals only 3 became pregnant. The grafts soon changed into cysts with a wall of connective tissue. Ovarian tissue very often could no longer be detected. It may be that the normal ovaries destroyed the transplanted ones. Each animal in which ovary had been transplanted had a very small infantile uterus. Though the normal ovaries contained corpora lutea the glands of the uterus were not at all developed, the submucosa also was poorly developed and the muscles were very thin. Perhaps the secretion of the normal and of the transplanted ovary neutralize each other, if this is true, one can believe that the ovary does not produce enough hormones to cause the development of the uterus, since the hormones are destroyed at once by the hormones of the graft —J K

(GONADS) Experimental alteration of sex in the Triton alpestris (Changement expérimental du sexe chez le Triton alpestris) Champy (C), Compt rend Soc de biol (Par), 1921, 172, 1204-1207

Two male Tritons, reduced to a sexually neutral condition by starvation, and then well fed, took on the external characteristics of females. One was killed, and was found to have fatty bands, with scattered indifferent spermatogonia, in place of testes. The other was killed 3 months later, and was found to possess ovaries lying medially to the degenerated testes. This observation is contrary to the theories of the predetermination of sex —Physiol Abst

(GONADS) Two cases of total genital infantilism (Deux cas d'infantilisme total de l'appareil génital) Chauvin & Vigne, Comité méd d Bouches-du-Rhone, 1922, abst, Presse méd (Par), 1922, 30, 596

Two women, normal in other respects, had infantile genitals. The ovaries were small and insufficient, the uterus of pubescent type, the vagina short and narrow and the vulva glabrous and infantile. The authors believe that it is very rare that these women have a normal general organic development —R G H

(GONADS) Use of lutein solution hypodermically for the control of nausea and vomiting of pregnancy Coffey (T), Am J Obst & Gynec (St Louis), 1922, 3, 513-516

A clinical report of 62 selected cases in which this method was used, 88.6 per cent being improved. An average of six and a half injections per patient was given. The least number of injections was one and the highest was twenty-five. If the discomfort was severe, the injections were given daily, but usually they were given every other day. No control study of cases by other methods was apparently made —E N

The INTERSTITIAL cells of the TESTICLE and the secondary sex characteristics in the fish (*Glande interstitielle du testicule et caractères sexuels secondaires chez les poissons*) Courrier (R), *Compt rend Soc de biol (Par)*, 1921, 85, 42-43

In the male stickleback the secondary sexual characteristics appear at the middle of April. At this time the formation of spermatozoa has ceased, and the interstitial cells of the testis show indications of secretory activity —Physiol Abst

(GONADS) Dystrophy adiposogenitalis and geroderma in dementia precoc (*Syndrome adipo-génital avec gérodermie chez un dément précoce*). Demole, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 605

Anatomical examination showed neither hypophyseal nor tuberculous lesions, but important lesions of the interstitial cells of the testicles —R G H

(GONADS) On the relations between fertility and nutrition I The ovulation rhythm in the rat on a standard nutritional régime. Evans (H M) & Bishop (K S), J Metab Research (Morristown, N J), 1922, 1, 319-327

It is conceivable that certain nutritive régimes may permit growth to occur and yet may prevent or interfere with the cyclic ovulatory mechanism. Good general growth or weight maintenance signifies a satisfactory ovulatory mechanism, but not necessarily the ability to bear young. Ovulation, when compared with implantation and placental function, is a relatively hardy mechanism and much if not most sterility must be traced to uterine failure. The authors report the study of several series of rats from the standpoint of the influence upon the length of the oestrous cycle of a standard diet as

compared with a generous table scrap diet. The microscopic criteria determined by Lang and Evans for the detection of oestrus were adhered to, and the ovulation rhythm was observed for a period of about 50 days. In both series, from 74 to 80 per cent of the oestrous cycles observed in animals on either of the nutritive régimes were of the normal four or five days duration, the adequacy of the standard diet thus seeming assured. This diet consisted of wheat (whole ground), 67.5, casein, 15.0, whole milk powder, 10.0, sodium chloride, 1.0, calcium carbonate, 1.5, butterfat, 5.0 —E N

(GONADS) *Hermaphroditism in a woman of 22 years, having feminine appearance and masculine characteristics (Hermaphroditisme chez une femme de vingt-deux ans ayant un état civil et un emploi masculins)* Fourguet & Coquet, Soc de méd & de chir de Bordeaux, 1922, abst, J de méd de Bordeaux, 1922, 94, 282

The patient began menstruating regularly at 14. The general appearance was feminine, but the clitoris was 4 cm long and the vaginal orifice minute. No uterus could be palpated —R G H

(GONADS) *The ovarian function* Graves (W P), Am J Obst & Gynec (St Louis), 1922, 3, 583-591

Cessation of ovarian function, as a result of operation, radium or the natural menopause, produces cessation of menstruation, local atrophy of the external genitalia, and temporary vasomotor disturbance. Cessation of menstruation as a fact per se has no specific permanent effect on a woman's general organism. Abnormal post-operative atrophy of the external genitalia is a rare occurrence, and is no more frequent after hysterio-oophorectomy than after the natural menopause. Vasomotor disturbances occur in about 80 per cent of cases, with equal frequency after castration and radiation. There is no reason for the patient to fear the acquisition of abnormal fat when the operation has been performed after full maturity. From such observations the author concludes that after constitutional maturity the chief province of the ovary is one of reproduction and that as an organ of internal secretion it is otherwise comparatively unimportant. Until the age of complete physical and mental maturity (on an average of 22 years), the ovaries are of great importance and should be sacredly preserved, both for their reproductive and secretory value. In the decade following full maturity the integrity of the ovaries should be carefully guarded, for this is the most important child-bearing epoch of the woman's life. During this decade conservation should be observed as far as possible, but if radicalism seems necessary for the patient's welfare, it may be practiced without fear of injury. Toward the latter part of the fourth decade, and even more after the age of 40, the importance of the ovary as an internal secretory gland becomes less and less until, by the age of 45, it need scarcely be regarded at all, except from a purely sentimental standpoint. Graves does not believe in

leaving the ovaries in situ in operations where the removal of the uterus is necessary —E N

(GONADS) Genital organs of hermaphroditic fur seals Hanna (G),
Am Naturalist (N Y), 1921, 55, 473-475

Two cases of false hermaphroditism in the fur seal are reported. One was preponderatingly male and the other female. The endocrine significance is not discussed —W J A

GONADS and senility (Keimdrüsen und Alterszustand) Harms
(W), Fortschr d Naturwissensch Forsch (Berl & Vienna),
1922, 77, 189-298

An excellent general review on this subject. Bouin, Ancel, Steinach and others have exaggerated the importance of the interstitial cells. They reported that sperm cells have no endocrine function. Plato, Kyrle, Stieve, etc., on the other hand, believed that the interstitial cells are only trophic elements for the sperm cells. Steinach has stated that a certain parallelism exists between the number of interstitial cells and the intensity of the secondary sexual characteristics and that autoplastically grafted testicles remain infantile, have no sperm cells and therefore show their endocrine function by the interstitial cells. This, however, has not been proved, as the grafted testicle contains many unripe spermatogones and Sertoli's cells to which the endocrine function may be attributed. The same is true with testicles transplanted in castrated female animals. Harms always found Sertoli's cells or cells derived from those in the graft. Some animals are without interstitial cells (testicle of the worms, ovary of amphibia and Bidder's organ in toads) and with secondary sexual characteristics. It is, however, quite possible that the interstitial cells have an endocrine function. The author often observed in histological pictures that interstitial cells gave substances to the capillaries. He believes that the endocrine substance of the testicle is made by degenerating or secreting spermatogones and Sertoli's cells, that it is kept in the interstitial cells in the form of a "Prosekret" and that in these cells this "Prosekret" is changed into the real "Sekret". In Bidder's organ, especially, many structures are found which sustain this theory —J K

(GONADS) Artificial glycosuria and its importance in the early diagnosis of pregnancy (Über Künstlich erzeugte Glykosurien und ihre Bewertung für die Frühdiagnose der Gravidität in der Praxis) Hellmuth (K), Klin Wchnschr (Berl), 1922, 1, 1152-1153

The author compared 3 tests for pregnancy. According to the Frank-Nothmann test, when 100 gm of glucose are given on an empty stomach to a pregnant woman glycosuria without hyperglycemia occurs. According to the Kamnitzer-Joseph test the injection of 2-2.5 mg of phloridzin on the empty stomach in pregnant women produces glycosuria. In the Roubitschek test 10 gm of

glucose are given on the empty stomach Twenty minutes later 0.5 cc of a solution of suprarenal 1:1000 is injected and glucosuria without hyperglycemia is found in pregnancy The Kamnitzer-Joseph and the Roubitschek test are of no value, the first one is often positive in women who are not pregnant and the second is never positive The Frank-Nothmann test is rather reliable Among 115 women who were not pregnant it was positive only 5 times
—J K

(GONADS) Hormonal sterilization of female animals through subcutaneous transplantation of OVARIES of pregnant females (Ueber hormonale Sterilisierung weiblicher Tiere durch subcutane Transplantation von Ovarien trachtiger Weibchen) Haberlandt (L.), Arch f d ges Physiol (Berl.), 1922, 194, 235-270

Of 8 rabbits into which ovaries of pregnant rabbits had been transplanted subcutaneously 5 showed a varying sterilization of almost 3 months' duration, while 3 were not markedly affected Of 8 guinea pigs 4 gave negative results, 3 showed a delayed conception of 3 to 4 weeks, and the eighth no conception after 10 months (perhaps due to other causes) In similar experiments the transplanted ovaries were examined histologically at varying periods of from 1 to 10 months The greater part of the organ remained, especially the interstitial cells (Two experiments each on rabbits and guinea pigs with corpus luteum optone injections gave negative results) Haberlandt suggests that this method of inducing partial sterilization may have some subsequent application in practical medicine —A T C

(GONADS) Chlorosis and illustration of a case of male chlorosis (Betrachtungen über Chlorose im Anschluss an die Demonstration eines lehrreichen Falles von viraler Chlorose) Holler (G.), Folia hæmatol (Leipz.), 1922, 27, 221-250

Description of a boy of 17 with tuberculosis and typical chlorosis The author believes that these two diseases are independent He also states that in woman chlorosis is caused by dysfunction of the interstitial cells of the ovary It is astonishing, therefore, that it is so rare in men, for one would expect that dysfunction of the interstitial cells of the testicle would produce male chlorosis Perhaps very light cases of chlorosis are not rare, but are not recognized It is also possible that the eunuchoidism before the onset of puberty in boys is equivalent to chlorosis in girls Such boys often have sisters with chlorosis The author concludes that the dysfunction of the "Pubertätsdrüse" is responsible for chlorosis in man as well as in woman —J K

(TESTES) The Russian-Roumanian castrated sect of Skopzi (Über die russisch-rumanische Kastratensekte der Skopzen)

Koch (W), Veroff a d Kriegs-u Konstitutionspathol, 1921, 2, 1-39

See Endocrin, 1922, 6, 410-411 —W J A

(GONADS) Two cases of hermaphroditismus verus (Zwei Falle von Hermaphroditismus verus) Kolmer (W) & Scheminsky (F), Arch f d ges Physiol (Berl), 1922, 194, 362-364

Egg cells have been found in the testis of a specimen of *Esox lucius* and also in a specimen of *Salamandra maculosa* —A T C

(GONADS) Function of the interstitial cells of the TESTICLE (Die Funktion der Zwischenzellen des Hodens) Jaffé (R), München med Wchnschr, 1922, 69, 873

A short note When spermatogenesis is disturbed the interstitial cells may increase or decrease in number The interstitial cells have a trophic and a resorptive function, but they probably have an endocrine function also, correlating with the other endocrine functions of the body —J K

(GONADS) Are there interstitial cells only in higher vertebrates (Finden sich Zwischenzellen nur bei den höheren Wirbeltieren)? Kolmer (W) & Scheminsky (F), Arch f d ges Physiol (Berl), 1922, 194, 352-361

Interstitial cells have been found definitely in the cyclostome *Myxine*, the holocephaloid *Chimaera monstrosa*, the elasmobranch *Torpedo marmorata*, and the teleosts *Myrus* and *Esox lucius*, and with great probability in *Raja punctata* and *Cepola rubescens* In a number of other fishes the amount of material available was small, interstitial cells were not found and further experiments are being made Taken in conjunction with Courrier's results (Endocrin, 6, 338), these lead to the conclusion that at any rate at times male gonads of all vertebrates contain interstitial elements —A T C

(GONADS) A case of painful gynecomastia cured by radio-therapy (Un cas de gynécomastie douloureuse guérie par la radiothérapie) (Laederich & Le Goff, Bull et mem Soc méd des hôp de Par, 1922, 46, 764-767

A man of 77 years who gave a history of acute blennorrhagia without orchitis at 20 years of age presented a bilateral mammary enlargement of a year's duration The right gland was slightly more enlarged than the left and was some 12 cm in diameter The nipples were prominent and surrounded by pigmented areolar tissue The skin was normal The glands were firm like those of a pubescent maid and well lobulated The testicles were normal on inspection and the patient was sexually potent Radio-therapy was given on one side A cold abscess of the breast developed on the untreated side The breasts before treatment were excruciatingly painful

Continued radio-therapy obliterated the pain and caused a diminution in the swelling —F S H

(GONADS) Women with penis Loeser, Klin Wchnschr (Berl), 1922, 1, 1283

From their 10th year two sisters showed development of a penis and a masculine distribution of hair Pneumo-radiography of the abdomen disclosed probable hypertrophy of both adrenals There were pathological changes in the sella turcica —J K

(GONADS) Hermaphroditism as an endocrine disturbance (*Hermaphroditismus als innersekretionische Störung*) Loeser & Israel, Deutsche med Wchnschr (Berl), 1922, 48, 853

Demonstration of two sisters with pseudohermaphroditism The inner organs were female, as was seen after a laparotomy, the vagina was very small, each sister had a large penis but a female psyche Pneumoradiography of the region of the kidneys showed enlarged adrenals —J K

(GONADS) Steinach's operation versus rejuvenation (*L'opération de Steinach peut-elle réaliser le rajeunissement de l'organisme animal*)? Marinesco (G), Presse méd (Par), 1922, 30, 309-311

Marinesco questions the applicability of the term "rejuvenation" to the results obtained by Steinach's ligation of the ejaculatory ducts and thinks that the cells of Leydig have no claim to the title of "puberty gland," although they doubtless secrete a specific hormone His own experiments show the presence of a characteristic biochemical substance in the cells of Leydig, revealed by their staining reaction to benzidine and hydrogen peroxid (peroxidase reaction), whereas the oxidase reaction, produced by the use of dimethylparaphenylenediamin and alpha-naphthol, only occurs in the reproductive cells, a fact which proves that a chemical difference between the two types of cells exists He points out that senility, on the other hand, is a very complex process, which causes fundamental changes in the chemistry of all the tissues, and especially in the colloid constituents of all the body cells Since it is known that both colloids and enzymes are subject to senescence, that the "ageing" of colloids, globulins, serum albumen, carbohydrates and lipoids is characterized by dehydration, degeneration and precipitation, and that the degeneration of albuminoids is an irreversible process, the mere retention of one or more hormones cannot be said to bring about rejuvenation Marinesco discusses the changes wrought in three patients (a tabetic and two patients with Parkinson's disease) to prove that the results obtained were merely a transient improvement of the pathologic symptoms during two months and an equally transient revival of sexual activity, but that neither the ataxia of the tabetic, nor the Parkinsonian symptoms were permanently relieved Temporary reactivation of certain physiologic functions should not be described

as "rejuvenation," which would require profound, complete and unattainable changes in the entire organism—G L

(GONADS) Dysgenitalism in two brothers (Dys-genitalismus bei two Brudern) Mayer (C), Klin Wchnschr (Berl), 1922, 1, 244

See Endocrin, 1922, 6, 435—J K

Vitreous hemorrhage at MENSTRUATION Meanor (W C), Penn M J (Harrisburg), 1922, 25, 494

Case report of a married woman, aged 33, in whom hemorrhage into the vitreous humor occurs at every menstrual period. The hemorrhage usually begins on the second day of menstruation. The vitreous becomes so cloudy that the fundus cannot be seen, but clears up before the next period. The patient has had blurred vision during her periods ever since menstruation began. She is the mother of two children and had the hemorrhage every month during her pregnancies. There has been no epistaxis—H L

(GONADS) The importance of the lipoids in the human OVARY (Ueber die Bedeutung der Ovariallipoiden) von Mikulicz-Radecki (F), Munchen med Wchnschr, 1922, 69, 851-854

In cells which function and which are in a state of development (egg cells, granulosa cells, theca cells in the follicles and lutein cells of the gravid corpus luteum) cerebrosides, phosphatides and other complicated lipoids are found. When these cells begin to lose their function (e g, thecal lutein cells in an atretic corpus) neutral fats are found in them and the lipoids gradually disappear. The last remains of such cells are masses of neutral fats, fatty acids and soaps. The author believes that the lipoids are endocrine products formed by the lutein cells immediately before fecundation and during the first of pregnancy. The experimental work of Iscovesco, Fellner, Herrmann, etc, have proved that it is possible to extract from the ovary complicated lipoids which, when injected, produce symptoms closely resembling those of beginning pregnancy—J K

(GONADS) A study of testis and ovary grafts on the hen's egg and their effects on the embryo Minoura (T), J Exper Zool (Phila), 1921, 33, 1-63

A study of nearly 600 eggs in which grafts of testis or ovary were made on the chorio-allantoic membrane. Modifications of the reproductive organs of the hosts took place, giving forms that were intermediate between the male and female. The sizes of gonads and the persistence of the Mullerian ducts were considered particularly. The author concludes that the differentiation of one sex is stimulated by the presence of a graft of the gonad of the same sex and inhibited by a graft of the opposite sex—M M H

On the physiological properties of the GONADS as controllers of somatic and psychical characteristics IV Gonad transplantation in the guinea pig Moore (C R), J Exper Zool (Phila), 1921, 33, 365-391

A study of over 50 guinea pigs of both sexes which have undergone complete castration at the age of 10 to 20 days. Gonads from animals of the opposite sex were implanted in these castrated individuals, repeated grafts being made in many cases. The presence of ovarian grafts in the male led to hypertrophy of the teats, while a graft of testicle in the female caused a pronounced modification of the clitoris towards the male condition. The psychical characteristics of the females were so modified that the animals behaved like males, but the reverse effect was not observed in the males, which retained their normal psychical characters —M M H

(GONADS) Interstitial cells and dementia praecox I Mott (F W) & Such (M P y), II Such (M P y), Proc Roy Soc Med (Lond), 1922, 15, 1-14, 14-30

Fully illustrated articles on the morbid histology of the testis. Changes in the reproductive organs form "a part of a generalized defect of durability and vital energy in the whole body most manifest in the brain, especially the cortex and the reproductive organs"

—Physiol Abst, 7, 130

(GONADS) Changes in the interstitial tissue of the TESTICLE in consequence of deficiency in water-soluble accessory substance B (Sulle modificazioni del tessuto interstiziale in seguito a deficienza di vitamina B nella dieta) Novaro (P), Boll d Accad med di Genova, 1920, abst, Pathologica, 1920, 12, 405

The testicles of four young pigeons, kept for two months on a diet of polished rice, were examined histologically. Material was fixed partly in Zenker and partly in Flemming. The testicular tubules were found atrophic, and their epithelium degenerated in many places. The intertubular spaces were larger than in normal specimens and filled with interstitial cells. These, instead of appearing isolated or in small groups of two or three, were arranged in well delimited rows supported by flattened connective tissue elements. The interstitial cells had increased, not only in number, but also in size, their nuclei being also larger than those of normal cells. In the specimens fixed in Flemming's fluid the cytoplasm of such cells appeared filled with many granules stained deeply black. The author comes to the conclusion that deficiency of the water-soluble accessory food factor B, causes a true hypertrophy and hyperplasia of the so-called interstitial gland of the testicle.

—Med Sc, 1921, 4, 168

(GONADS) The physiology of the TESTIS (Contribución experimental para el estudio de la fisiología del testículo Segundo

memoria) Ocaranza (F), Rev Mex de biol (Mexico), 1922, 2, 219-235

This is a continuation of the work on guinea pigs reported a year ago (Rev Mex de biol, 1921, 1, No 6) and deals with the effect of castration and testicular grafting on the number of blood corpuscles per unit volume of blood. The previous report was based on 4 complete and 3 incomplete castrations from which the author made the tentative deduction that the blood changes which resulted might be due to some general metabolic disturbance produced by the absence of some testicular autacoid that influences the hemopoietic organs. The number of additional animals studied is not stated, but there is given the protocol of 6 individuals for a period of several days before double castration to about a month after. These experiments, like the previous ones, showed a constant decrease of various degrees in both red and white corpuscles just after castration, followed by an increase frequently to above normal and then waves of alternate decrease and increase—the rise in the white count coming a little ahead of the corresponding increase in the red. The leucocytosis is largely due to neutrophils with a tendency towards lymphocytic adjustment. Since eosinophilia was observed in only 2 cases to follow immediately after the operation and in one case 15 days after, and since the changes in the blood count occur in waves, the author is now inclined to think that the variation is not due to general metabolic disturbances, but rather that some organs are constantly connected with blood formation and others are only occasionally thus involved. In the absence of the former the corpuscles decrease to a limit compatible with physiological equilibrium and then the latter organs begin to influence blood formation, whereupon the bone marrow becomes stimulated to increased hemopoietic function. The variations in the blood count and in the behavior of the animals produced by grafting testicular tissue into both castrated and non-castrated males and into pregnant females are recorded in 10 cases. The results were variable so that no particular conclusions are drawn. The author realizes that a disturbing factor might be the rapid absorption of the grafted tissue which might act as foreign protein. He noted, as others have done, that castrated animals with iso- or homo-grafts retained the sexual instincts. Some became more than usually aggressive after absorption of the graft. Testicular grafts did not change the maternal instincts of non-castrated females. The grafts, one month after implantation, showed an almost complete disappearance of the interstitial (“diastemática”) gland. The germinal epithelium in each tubule formed a flocculent colloidal complex in the center of which were remains of nuclei and spermatozoa. Grafts from which the tunica albuginea had previously been removed were enveloped in a delicate connective tissue capsule similar in appearance to the original tunica albuginea. Fourteen references are given.—A T R

(GONADS) Hen feathering in cocks Pease (M S), Proc Cambridge Phil Soc, 1922, 2, 22-26

Morgan attributes suppression of cock-feathering in hens and in cocks with hen-feathering to the presence of luteal cells in the generative organs The author finds these cells present in all cocks except when spermatogenesis is in full swing The cells form most likely a food supply for sperm formation, and were absent from the 2 birds (on which Morgan apparently bases his theory) he examined, because spermatogenesis was inactive —Physiol Abst, 7, 262

The so-called INTERSTITIAL tissue in the testis of the urodele batrachian (*Sur un prétendu tissu interstitiel dans le testicule des batraciens urodèles*) Pérez (C), Compt rend Acad d Sc (Par), 1921, 172, 1443-1445

The tissue in the testis of Triton, described as interstitial by Champy, has nothing in common with the interstitial cells of the mammalian testis It is due to phagocytic changes in the testicular tissue proper —Physiol Abst, 6, 327

(GONADS) Numerical law of regression of certain secondary sex characters Pézard (A), J Gen Physiol, 1921, 3, 271-283

Postpubertal castration is followed in cocks by a regression of the comb In a few weeks the aspect and dimensions of this organ is similar to that of cocks castrated before puberty Eight animals were used —H A McC

(GONADS) Epilepsie et fonctions OVARIENNES Rebattu, Mollon & Sédailhan, Bull Soc méd d hôp de Lyon, 1922, abst, Presse méd (Par), 1922, 30, 620

The authors have studied the reports on a number of patients in the hospital at Perron on the relation between epilepsy and the genital life in a woman They studied the influence of the establishment of menstruation on the first crises, the influence of the first menstruation on the crises existing previously, the coincidence of the rises and the menstrual periods, the influence of the cessation of menstruation on account of pregnancy, castration and the menopause, and the results of ovarian organotherapy They concluded, in spite of the complete failure of ovarian medication, that in about a third of the cases there was a slight relation between epilepsy and functions of the ovary The menopause often leads to disappearance of the crises or diminution of their frequency, but the first crises sometimes appear at the menopause In this case the relation between epilepsy and the genital functions remains through life In 3 patients the first crises appeared at puberty, causing their menstrual periods to come to an end, as in the menopause Other endocrine troubles, such as disorders of adrenal, hypophysis or thyroid origin are not involved The internal secretion of the ovary seems to be

the only one which plays a rôle in epilepsy, and, moreover, this is inconstant —R G H

(GONADS) Primary sterility A study based on 400 cases Rongy (A), Am J Obst & Gynec (St Louis), 1922, 3, 553-556

The various causes of sterility are discussed, the author warning against the "blind acceptance of the theory that the organs of internal secretion are responsible for sterility" The treatment of sterility consists chiefly in being able to select the patients who are likely to respond to treatment Those patients with congenitally defective organs should be left alone —E N

TESTICLE transplantation (Hodenüberpflanzung) Rosenthal, Munchen med Wchnschr, 1922, 69, 137

See Endocrin, 1922, 6, 457 —J K

(GONADS) A special type of atresia of the graafian follicles of the rabbit as revealed by the tanno-ferric method [Sur une forme particulière d'atrésie des follicules de De-Gräaf (lapine), révélée par la méthode tanno-ferrique] Salazar (A L), Am J Anat (Phila), 1922, 30, 503-523

This special type of atresia is to be observed in the small follicles of the ovary of ovigenic type, and is characterized by the formation in the interstices of the cells of the granulosa of a long tannophilic cord The author examines the connection of this type of atresia with hydropic atresia in the ovigenic cords and its remains (epithelial nodules, anova follicles of Regaud), recently described by him, and discusses the significance of the cases described

—Abst, Wistar Institute

(GONADS) Convulsive and anticonvulsive action of the genital hormones (Azione convulsivante ed anticonvulsivante degli ormoni genitali) Sanchirico (F), Folia med (Napoli), 1922, 8, 161-167

Epilepsy is said to be due in many cases to the action of hormones in the nervous system This is indicated indirectly, according to Sanchirico, by the resemblance between the convulsions produced by hormones (especially genital) and those caused by strychnia The data, however, are equivocal The author injected into rabbits gonad extracts sufficient to produce convulsions and studied the influence of the dosage factor Usually positive results were obtained —P M N

(GONADS) Modern experimental sexual research, especially the recent experiments of Steinach ("rejuvenescence") [Moderne experimentelle Sexualforschung besonders die letzten Versuche Steinachs ("Verjüngung")] Sand (K), Ztschr f Sexualwissenschaft (Berl), 1920, 7, 177-197

An exceptionally lucid and well organized review and discussion of the subject with considerable emphasis upon the work of Steinach and similar experiments, upon which Sand is well qualified to speak, having for several years been engaged in similar investigations

—A T R

Changes in the vaginal epithelium of the guinea pig during the OESTROUS CYCLE Selle (R), Am J Anat (Phila), 1922, 30, 429-449

A syringe method for taking vaginal samples is given as being more satisfactory than any other method yet used Its use in testing the cellular contents of the vagina during the various stages of the oestrous cycle of the guinea pig is described The length of the oestrous cycle for this animal was found to average 15.87 days, which corresponds closely to the determination of Stockard and Papanicolaou Four well-defined periods or stages, in addition to the interval, are recognized for the complete cycle —W J A

(GONADS) Modification of the indications for operative interference in gynecology imposed by present radium therapy Skeel (R), Northwest Med (Seattle), 1922, 21, 131-136

Menorrhagia, especially the menstrual hemorrhages of the adolescent period, are probably often due to endocrine disease, more particularly ovarian instability or overactivity Radical surgery should be abandoned in these cases Radium in doses that will temporarily stop menstruation is the treatment of choice The remainder of the article though excellent is not of endocrine interest

—H L

Influence of injections of foetal, placental and uterine extracts on the gravid CORPORA LUTEA in the hysterectomized guinea pig (*Influenza delle iniezioni di estratti fetali, placentari, uterini sui corpi lutei gravidici di cavie isterectomizzate*) Verdozzi (C) & Cavalieri (R), Arch di fisiol (Firenze), 1920, 18, 1-13

Subcutaneous injections of aqueous extracts of guinea pig embryos into guinea pigs on which hysterectomy had been performed during the first half of pregnancy present, up to a point, the rapid involution which the corpora lutea undergo when hysterectomy only is performed Under the same experimental conditions, injections of placental and uterine extracts have no effect of the sort This appears to support Verdozzi's opinion that the persistence of the corpus luteum during pregnancy is, at least in part, due to "chemomorphotic" substances passing through the placenta from the embryo to the mother —Physiol Abst

(GONADS) Influence of x-rays on the sex glands (*Über Geschlechtsbeeinflussung durch Röntgenstrahlen*) Welloch (J), Strahlentherapie (Berl u Wien), 1921, 13, 114-125

Experiments on animals and statistics from men show that an influence on sex by irradiating the sex-glands with x-rays does not exist —Physiol Abst, 7, 131

Structures and homologues of free-martin GONADS Willer (B H), J Exper Zool (Phila), 1921, 33, 63-129

Free-martin gonads show three degrees of transformation in the male direction. These transformations involve the sexual cords, interstitial cells, rete, epididymis, and the distribution of the blood vessels. The transformed gonad may be a morphologically complete testis, but spermatozoa are never formed. Although hypertrophy of interstitial cells may occur it is here independent of atrophy of the male germ cells, and does not influence secondary sexual characters or instincts —M M H

(GONADS) Phlorizin glycosuria and the diagnosis of pregnancy (Phloridzinglykorurie und Schwangerschaftsdiagnose) Zondek (B), Zentralbl f Gynäk (Leipz), 1922, 46, 851-853

If, after injection of 2 mg of phlorizin no glycosuria is seen, it is highly probable that the patient is not pregnant —J K

La pituitrina. Barbabosa (A V), Observador Med, 1920, 2, 326-332

A general discussion of the pharmacology of pituitrin with special reference to the uterus —R G H

Technique, résultats et indications de la radiothérapie dans les tumeurs de la région HYPOPHYSAIRE Bécère, III Réunion neurol internat, Paris, 1922, abst, Presse méd (Par), 1922, 30, 616

Practically for the first time in 1907 radiotherapy was used for buccal irradiation. Gramegna had excellent success with this method. The frontal, parietal or temporal route can be used. There was already developed deep radiotherapy, and modern methods have improved its technique. There is now a way of indicating precise dosage, depth of irradiation and intensity of depth. The first two patients treated by Bécère were entirely cured. Since then 40 observations of hypophyseal tumors treated by radiotherapy have been reported by the author. The results were remarkable and included all the symptoms. There was improvement of vision and enlargement of the visual field (even after cessation of treatment), improvement of troubles due to intracranial hypertension, loss of excessive adipose tissue, reappearance of menstruation, arrest of development of osseous lesions in acromegaly, etc. Comparing the results of radiotherapy with other therapy, opotherapy or surgery, Bécère concludes that it is the treatment of choice for hypophyseal tumors, particularly in cases of acromegaly and gigantism, with the

exception of tumors of syphilitic origin and of syndromes of glandular deficiency—R G H

The action of the different extracts of the posterior lobe of the **HYPOPHYSIS** in the dog (Action des différents extraits de lobe postérieur d'hypophyse sur le chien) Béco, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 605

Contrary to the opinion of certain physiologists, hypophysis extract undoubtedly causes oliguria, and also cardiotoxic action. Thus the endocrine secretions of the hypophysis play a rôle in the preservation of the vascular tonus—R G H

Ueber die **HYPOPHYSIS** Biedl München med Wchnschr, 1922, 69, 796, Klin Wchnschr (Berl), 1922, 1, 1280

The old fashioned idea of the anatomy of the pars anterior and the pars posterior is not right. The pars intermedia, which is very small in man, is a specific tissue, another specific part of the hypophysis is the pars tuberalis, that is, the tissue of the hypophyseal stalk. The pars anterior and the additional glands find their origin in the roof of the throat (Rachendach), the rest of the pituitary is of ectodermal origin. The pars anterior is an endocrine organ and its secretion is in the form of lipoids and granula (basophil or eosinophil). It contains a lipoid, the tethelin. The active principle of pars posterior and intermedia are histamin-like substances. Removal of the gland may produce cachexia. Tumors of the pars anterior, causing an increased function, produce gigantism and acromegaly. The changes in metabolism, which are seen in these diseases, are due to changes in the pars intermedia. **Dystrophia adiposogenitalis** and **diabetes insipidus** may be caused by disease of the base of the brain as well as by a disease of the pars intermedia. There is still another disease, very little known, having its origin in the same part of the basis of the brain. Its symptoms are atresia ani, polydactylism, retinitis, albuminuria, dullness, adiposity and characteristic disturbances of growth—J K.

HYPOPHYSEAL syndromes (Les syndromes hypophysaires) Anatomie et physiologie pathologiques, Camus (J), Étude anatomopathologique, Roussy (M G), III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 604-605

A summary, largely of original work, on the problem. See *Endocrin*, 4, 507-522. Extensive discussion is reported—R G H

Tumeurs de L'HYPOPHYSE et troubles visuels Symptômes Radiothérapie Carlotti, Ann d'ocul, 1922, abst, Arch méd belges (Brux), 1922, 75, 228

Carlotti reports 4 cases of the hypophysis syndrome accompanied by visual disorders, after having studied the question from

the point of view of semeiology and treatment The chiasmatic syndrome with acromegaly or dystrophia adiposogenitalis is due to a lesion of the hypophysis, appearing often in old syphilitics—twice among the 4 observations From the point of view of early diagnosis it is necessary thoroughly to study the visual field If the Wassermann test is positive treatment may be tried but the case is usually hopeless As soon as possible the patient should be treated with x-rays, giving him the maximum tolerable dose If this does not appreciably affect the visual field at the end of a month the patient should be referred to a surgeon Organic treatment (extracts of ovary, thyroid, and hypophysis) may have a generally good influence—R G H

(HYPOPHYSIS) Tumeur du 3^e ventricule avec polyurie Chabrol & Gambillard, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 615

A case is reported of a tumor of the hypophysis which encompassed the chiasm, reached the tuber cinereum and encircled the pituitary stalk—R G H

Surgical treatment of HYPOPHYSEAL tumors (Le traitement chirurgical des tumeurs hypophysaires) Cushing (H), III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 615-616

This report, based upon 500 clinical observations of hypophyseal syndromes, takes no account of anything except verified tumors They represent 60% of the cases operated upon (210) In comparison with other intracranial tumors (780) they represent 20% of the cerebral tumors They are divided into 3 large groups pituitary adenomas, 154 cases, congenital tumors (pharyngeal sac), 35 cases, suprasellar tumors that are not hypophyseal, 20 cases In the clinic visual troubles are prominent manifestations, the ophthalmoscope, the perimeter and radiography are used in their examination By far the most important is the information furnished by the perimeter Successive records show the progression of the syndrome, and, above all, constitute the best criterion of the degree and the persistence of operative amelioration From the surgical point of view it is possible to divide the tumors of the hypophysis into two groups—the suprasellar, which are preferably treated by an intracranial operation, and the infrasellar, which may be approached through the nose (transphenoidal route) It is necessary to consider the immediate danger of the operation, and the degree and duration of amelioration which is to be expected Two hundred forty-three operations have been performed with a mortality of 10%, including the cases in which extirpation could not have been successful—giving in reality a mortality of 5% Operation by the transphenoidal route necessitates an incision at the level of the lig-

ment of the upper lip, the separation of the mucosa and of the septum, and ablation of a part of the septum and of the wall of the sphenoidal cells. A double speculum permits the carrying on of the rest of the operation under the control of sight. Of 154 cases of hypophyseal adenoma operated upon in this way, with more or less radical extirpation, marked amelioration followed in 50%, always with an enlargement of the visual field to the normal, amelioration with retardation of the malady occurred in 20% of the cases, and 20% already blind were not affected. The mortality was 8%. Operation by the transfrontal route involves a direct approach to the region of the chiasm by retraction of one of the frontal lobes. This is the preferable operation in all cases of suprasellar tumor, if the tumor is small it can be extirpated completely without wounding the chiasm thus affording permanent cure. Eleven of 27 cases of tumors of the pharyngeal sac operated upon in this way resulted favorably after the extirpation of cystic tumors. In 11 other cases the cyst was simply punctured and emptied and the period of amelioration was of short duration. In 5 cases the tumor was inoperable. Simple adenoma with excavated sella turcica can be extirpated by an operation by the lower route without great risk, and with hope of an immediate and lasting improvement of vision. Tumors of the pharyngeal sac should be attacked by the higher route, by osteoplastic craniotomy. Permanent cure can be expected only when the tumor has been extirpated. A remarkable series of projections illustrated the operative procedure and the history of a certain number of the cases.—R G H

Adénome basophile du lobe antérieur de L'HYPOPHYSE avec adiposité Demole, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 605

Demole invokes the rôle of compression of adenoma on the infundibular region to explain the development of adiposity

—R G H

Treatment of HYPOPHYSIS tumors (Zur Behandlung der Hypophysentumoren) Denker, Verhandl d Gesellsch deutsch Nasen-, Hals- und Ohrenärzte, 1921, abst, Schweiz med Wchnschr (Basel), 1922, 52, 549

The author describes a premaxillary approach to the hypophysis and reports three cases of tumors with bitemporal hemianopsia or blindness and other characteristic outstanding features. He undertook to bring about calcification by the injection of calcium lactate and Pregel's solution. Improvement followed in all three cases

—R G H

(HYPOPHYSIS) Tethelin—the alleged growth-controlling substance of the anterior lobe of the PITUITARY gland Drummond (J C) & Cannan (R K), Biochem J (Lond), 1922, 14, 53-59

An attempt was made to isolate tethelin according to the method of Robertson. The product obtained did not show the constancy in nitrogen and phosphorus content of Robertson's preparation nor was it white. In spite of these facts the conclusion is made that the substance "Tethelin" is a very impure mixture of lipoids. After severely criticising the statistical methods used by Robertson in his study of the effect of tethelin on the growth of mice the authors proceed to make a similar study of the effect of the impure mixture they prepared. Negative results were obtained, and the conclusion is drawn that the oral administration of anterior lobe of the pituitary gland is without influence upon the growth of mice —F S H

Tumeur HYPOPHYSAIRE d'origine hérédo-syphilitique Syndrome thyro-testiculaire consécutif Herpès labial récidivant Faure-Beaulieu & Georges, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 615

The authors report a case of myxodematous facies, of glabrous skin, with testicular atrophy and frigidity. There was also anterior hypophyseal disorder, characterized by blindness, bitemporal hemianopsia and an enlargement of the sella turcica. The patient was a heredosyphilitic —R G H

Extrait HYPOPHYSAIRE et diurèse Foix & Thevenard, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 616

Hypophyseal extract had in 4 cases of tuberculosis manifest oliguric action, in one case it was without action and in another it produced slight increase in diuresis —R G H

(HYPOPHYSIS) Progressive muscular dystrophy Friedman (E D), J Nerv & Ment Dis (N Y), 1921, 54, 294-297

A case of a boy of 16, with distinct muscular dystrophy, and showing some pituitary involvement, gave normal blood sugar content, attributed to the fact that the patient was still active
—Chem Abst, 16, 744

Les syndromes HYPOPHYSAIRES Études clinique et thérapeutique Froment (M J), III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 606-607

A summary of the present status of the problem, not amenable to abstracting. Extensive discussion is reported —R G H

La thérapeutique des syndromes HYPOPHYSAIRES Froment (J) III Réunion neurol internat ann, Paris, 1922, abst Presse méd (Par), 1922, 30, 616

Radiotherapy is of equal importance with surgical treatment. Since the work of Gramegna and above all of Bécère it has given

remarkable results in the treatment of tumors of the hypophysis. As regards opotherapy, hypophyseal extracts should not be considered as equivalent to products secreted by the hypophysis. Two modes of action can be distinguished, namely, opotherapeutic and toxico-dynamic, but it is very difficult at present to indicate what results from the one or the other. We do not definitely know whether the histamine, discovered by the chemists, in the extracts used in therapeutics exists in the fresh gland. Different extracts used in the clinic vary greatly in their activity. We are still ignorant of the posology of these products. There is only one syndrome in which injections of extract of the posterior lobe have had a marked effect, namely, diabetes insipidus, but it seems to have a palliative rather than a curative action. When administered by mouth it is very much less active, due to the destructive action of digestive juices, especially the pancreatic. Its efficacy is increased when it is injected intraspinally. Some encouraging results, but rarely a complete cure, have been obtained in infantilism and dystrophia adiposogenitalis. There is increase in stature, growth of hair, reappearance of menstruation and sexual instincts and sometimes with extract of the anterior lobe even a loss of 25-50 pounds in weight. In acromegaly and gigantism organotherapy seems to be contra-indicated, but it is not always fatal.—R. G. H.

The regulation of the use of sublimate and **HYPOPHYSEAL** preparations by mid-wives (*De la réglementation de l'emploi par les sage-femmes du sublimé et des extraits hypophysaires*) Fruinsholz, Remy & Job. Bull. Soc. d'obst. et de gynéc. de Par., 1922, 11, 36-38.

A discussion favoring limitation of use of hypophyseal preparations to physicians.—F. S. H.

(**HYPOPHYSIS**) Two cases of pituitary tumor with acromegalic syndrome cured by x-rays (*Due casi di tumore dell' ipofisi con sindrome acromegalica curati coi raggi X*) Gavazzeni (S.), Radiol. med. (Torino), 1920, 7, 222.

One case had the complete clinical picture of acromegaly, and radiographically showed evidence of pituitary tumor. The symptoms of disease were of four years' standing, but the condition improved very much under x-ray treatment. The other case showed the same symptoms and signs in a milder degree, and the results of radiotherapy were equally good.—*Med. Sc.*, 1921, 3, 476.

Secretory activity of anterior lobe of **HYPOPHYSIS** during pregnancy (*Sull' attività secretiva della preipofisi in gravidanza*) Gentili (A.), *Sperimentale Arch. di biol.* (Firenze), 1920, 74, 286.

In large part a confirmation of known facts. The pars anterior progressively increases in cows from the beginning to the end

of pregnancy The weight of the hypophysis in multiparous cows is 135 to 140 mgm , at the beginning of pregnancy, 170 mgm , at the end, 350 mgm In multiparous cows it may weigh 460 mgm In these animals the pars anterior is excellent material for the "gravidic" cells, whose function is to secrete lipid substances, possibly phosphatids During pregnancy also the chromophobe cells appear to secrete great amounts of colloid —Physiol Abst

DIABETE insipide et opothérapie HYPOPHYSIAIRE Gilbert (A), Villaret (M) & Saint-Girons (F), III Réunion neurol internat , ann , Paris, 1922, abst , Presse méd (Par), 1922, **30**, 616

A case is described of an Italian of 31 years who, 2 years after having hemiplegia of syphilitic origin, began to be troubled with typical diabetes insipidus, with marked obesity Daily, subcutaneous injections of posterior lobe of the hypophysis reduced the diuresis to normal and produced a loss of 2 kg in weight But this therapy gave no results after specific treatment had ended and was without effect on the polyuria as well as the hemiplegia and obesity The authors believe that the diabetes insipidus was not of nervous, but of hypophyseal origin, they based their view on the remarkable efficacy of the organotherapy, the absence of effect on polyuria of rachicentesis and the non-existence of clinical or biological signs of a nervous infundibular lesion —R G H

(HYPOPHYSIS) The pigmentary effector system I Reaction of frog's melanophores to pituitary extracts Hogben (L T) & Winton (F R), Proc Roy Soc , 1922, **93**, 318-329

The posterior lobe of the pituitary contains a specific stimulant which, if injected into the frog, brings about general and complete expansion of the dermal melanophores, a dose equivalent to 1 0003 to 0 0005 cc of commercial "infundibular" preparations is sufficient to induce a darkening of the skin visible to the naked eye This stimulant is not destroyed by pepsin or boiling, it is not identical with histamine, since neither histamine nor putrid meat extracts give this reaction It is rapidly destroyed by trypsin It is not rapidly destroyed by acid hydrolysis (continuous boiling with 0 5% HCl), and in this respect agrees with the oxytocic (uterine) and differs from the pressor principle After cocaine, curare, atropine, and apocodeine it still evokes its characteristic response, and therefore acts probably directly upon the melanophores The result of the experiments confirms the endocrine significance of the condition of general pigmental contraction found by Allen and others to follow removal of the pituitary gland in tadpoles If Spaeth's observations are correct, the melanophores of amphibia and fish respond in an opposite manner to the pituitary autocoid, the action of the latter is also opposite to that of adrenaline in the amphibia

—Physiol Abst , **7**, 260

In a patient, aged 80 years, with polyuria and glycosuria histological study revealed a focus of the right suboptic region destroying the striated projection fibres and causing a deep lesion of the tuber cinereum. The hypophysis presented a unique malformation. The hypertrophic nervous lobe did not penetrate the sella turcica, but appeared to be joined to the intervening wall, giving the appearance of an infundibular tumor—R G H

The structure and differentiation of the specific cellular elements of the pars intermedia of the HYPOPHYSIS of the domestic pig Maurer (S) & Lewis (D), J Exper M (Balt), 1922, 36, 141-156

By use of the recent finer cytoplasmic stains the authors have demonstrated a specific type of granulation in cells of the pars intermedia. These are taken to be the true secretion antecedent for this part of the gland. The granules are smaller and stain blue and acid violet, but less intensely than any of the cells of the anterior lobe. They are very labile, disappear rapidly as a result of post-mortem change and dissolve readily in many fixing agents. The specific granules first appear in the hypophysis of embryos measuring 17.5 cm in length, at which time Lewis has demonstrated that the fetal hypophysis first forms a pressor substance. At this stage no colloid is present in the gland. Maurer and Lewis are inclined to controvert the Herring-Cushing theory by which the secretion of the pars intermedia is held to pass into the neural lobe and on through it to the third ventricle, and thus to circulate in the cerebrospinal fluid. They hold rather that the secretion leaves the gland by the vascular route—W J A

The effect of the extract of the posterior lobe of the PITUITARY on basal metabolism in normal individuals and in those with endocrine disturbances McKinlay (C A), Arch Int Med (Chicago), 1921, 28, 703-710

In 11 out of 12 normal persons, the subcutaneous use of pituitary extract increased the basal metabolic rate quite definitely. In 4 cases of hypothyroidism, the interesting phenomenon occurred of a reduction in the already low basal metabolic rate following subcutaneous injection of pituitary extract. In 3 cases of disturbed function of the hypophysis, without any clinical evidence of thyroid disturbance, subcutaneous injection of pituitary extract was followed by prompt and definite rise in basal metabolism. In another group, 4 normal persons were given thyroxin and one week later, subcutaneous injection of pituitary extract. All responded by increased basal metabolic rate over and above the rate increase from the thyroxin alone. Whereas in two cases of myxedema whose rates had been advanced by thyroxin, subsequent injection a week later of pituitary extract had no effect. McKinlay concludes that normal per-

sons and those with subnormal basal metabolism not due to thyroid deficiency, respond with accelerated heat production upon injection of pituitary extract, but that cases of hypothyroidism do not respond positively to such injection. There would seem to be a synergic action between thyroxin and pituitrin—H L

DYSPITUITARISM Report of a case of posterior lobe insufficiency controlled by organotherapy Morris (R S) & Weiss (H B), J Am M Ass (Chicago), 1922, 78, 1522-1523

Obesity, drowsiness, headache, frequent nocturnal urination, loss of sexual power and impairment of memory have been relieved and controlled for six years by posterior lobe extract. The detailed case report is given—W M A

PITUITARY disorders (Hypofyselidelser) Motzfeldt (K), Norsk Mag f Lægevidensk (Kristiania), 1920, 12, 1194-1216 (Summary in English)

The author reports five cases. A man of 54 had for many years shown the characteristic appearance of acromegaly, but had felt perfectly healthy. After a severe attack of typhoid fever he developed symptoms of diabetes mellitus—thirst, polyuria, considerable loss of weight, muscular weakness and glycosuria, but no ketonuria. Examination revealed an enlarged sella turcica, normal fields of vision and transitory hypermetropia. He improved remarkably during dietetic treatment, and was discharged after two months. His blood sugar had gradually decreased from 0.18 to 0.11 per cent. One month later he was taken into the hospital again to have his carbohydrate tolerance tested. He could then take 500 gm of bread and even 100 gm of glucose without glycosuria. It seems justifiable, therefore, to consider that the man was actually cured. In a woman of 25 the usual symptoms of acromegaly had developed gradually during 7 years. The sella turcica was enlarged and the fields of vision normal. The carbohydrate tolerance was lowered. In a woman of 32 the disease was of 8 years duration, from the start there had been marked pilosity. The chief symptoms were severe headache, hemianopsia and glycosuria, but no other symptoms of diabetes. The fact is emphasized that the disturbance in carbohydrate metabolism occurs only in pituitary tumors giving rise to acromegaly. The fourth case was a man of 38 whose skin was soft, with scanty growth of hair. Adiposity had started 10 years before and sexual activity had been abolished for many years. His complaints were chiefly of a neurasthenic nature. The sella turcica and fields of vision were normal. He could take 300 gm of cane sugar without glycosuria. Thyroid and especially pituitary extracts brought about marked improvement. During a relapse one month after his discharge from the hospital, considerable polyuria occurred, which disappeared spontaneously, however, after a few days duration. For the oral administration of pituitary preparations the importance

of big doses is emphasized Adiposity in a man of 64 began 15 years ago He has always been well and was not admitted to the hospital for his endocrine disturbance The growth of hair had always been very scanty The thyroid could not be felt distinctly The sella turcica and fields of vision were normal The testes were small and atrophic, there was no disturbance in sexual function His carbohydrate tolerance was between 100 and 200 gm of glucose There was marked reaction to adrenalin, but no reaction to pilocarpin It is uncertain whether this syndrome should be referred to a primary pituitary disorder or pluriglandular insufficiency

—R G H

(HYPOPHYSIS) Des troubles de sécrétion de la glande pituitaire
Pilatte (R), Progrès méd (Par), 1921, 36, 464-465

An historical epitome of the principal data regarding hypophyseal disorders —R G H

The action of HYPOPHYSIN, ergamine and ADRENALINE upon the secretion of the mammary gland Rothlin (E), Plimmer (R H A) & Husband (A D), Biochem J (Lond), 1922, 16, 3-10

A series of goats were used in these studies It was found that hypophysin produces a flow of milk only in the early stages of lactation Its action is rapid and powerful, but of short duration, and the flow then becomes less in quantity than normal The total volume of milk per day is not altered Since hypophysin does not act at later stages of lactation, it is probable that its action is indirect through the organs of reproduction The chemical composition of the hypophysin milk is not different from normal The secretory activity of the mammary gland is not affected by the subcutaneous administration of either ergamine or adrenaline The gland probably does not contain sympathetic or parasympathetic nerve fibers for the secretory mechanism If they be present the inaction of ergamine and adrenaline is exceptional —F S H

Studies on the effective principles in the extract of the PITUITARY body Saito (Y), Sei-i-Kwai M J (Tokyo), 1921, 40, 4-5

In view of discordant reports in the literature of hypophyseal pharmacology, Saito has added another experimental study Posterior lobes of horses and cows were extracted with saline solution (15) From such extract the following results were obtained It causes no dilatation of the pupil of the frog eye There is no color reaction to iron chloride solution, but a marked reaction to Pauly's histidin There is a vigorous contraction of a virgin guinea pig uterus, suspended in Ringer's solution, when a few drops of the extract are added After the intravenous injection of the extract the rise of blood pressure is not so rapid, its maximum is much lower and the decrement is more irregular than in the case of adrenalin

injection Boiling the extract in slightly alkaline solution completely destroys the pressor effect, while the depressor effect as well as the contracting action on the uterus remains undiminished With methyl alcohol and sulphuric acid the isolated substance shows intense Pauly reaction and retains its depressing and contracting effects After repeated extraction with chloroform of the pituitary extract, which was treated previously with trichloroacetic acid, there is rise of blood pressure only on the first intravenous injection, the effect diminishing after succeeding injections at short intervals and producing even decrease This pressor principle gives rise to the contraction of the uterine muscle, while adrenalin causes a marked relaxation of the uterus Though a mixture of histamin and adrenalin in equal amount has about the same effect on the uterus as does pituitary extract and neutralizes its bad effects, it would be reasonable to use the pituitary extract for obstetric practice because it contains no substance inhibitory to uterine contraction —R G H

Clinical history and pathological anatomy of a HYPOPHYSEAL tumor of 14 years standing, treated by radiotherapy (*Histoire clinique et anatomo-pathologique d'une tumeur hypophysaire datant de 14 ans, traitée par la radiothérapie*) Sainton & Schulmann, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 615

The histological findings are reported of a hypophyseal tumor, remarkable because of the duration of its development, and the predominance of signs of compression, contrasted with the slight endocrine reactions There was dystrophia adiposogenitalis Radiotherapy, which was used in 1910 led to the clinical cure of the patient, but he died of pneumonia The tumor weighed 60 gm It was an atypical epithelioma of the basophile cells of the anterior lobe Although occurring at a relatively young age, this hypophyseal lesion had only a slight effect in the other endocrine glands (persistence of the thymus, modifications of the thyroid, with, finally, sclerosis and hyperplasia and testicular hypoplasia) —R G H

ACROMEGALIE Secousse & Pesme, Soc de méd et de chir de Bordeaux, 1922, abst, J de méd de Bordeaux, 1922, 94, 399

A case of typical acromegaly is reported Radiographs shows a thickening of the cranial structure, of the frontal sinus, of the sphenoid and of the sella Treatment with extract of hypophysis has given no result, however, this is not surprising since hypophyseal hypersecretion must be present Concomitant glycosuria diminished with continued treatment of diabetes, but increased in the same manner as the persistent headache with the irradiation of the hypophysis Retinal symptoms, hemorrhages and white spots were noteworthy Relation has not yet been established between the latter symptoms and glycosuria, but has with albuminuria and cylindruria —R G H

(HYPOPHYSIS) The influence of pituitrin on the motor function of the bladder (*L'influenza della pituitrina sulla funzione motoria della vescica*) Serdinkoff (M G), *Riforma med* (Napoli), 1922, 38, 413-417

Following an exhaustive discussion on the action of the pituitrin on smooth muscles the author reports a case in which, besides subinvolution of the uterus (after miscarriage), peri- and parametritis, there was also inflammation of the bladder and impossibility to void urine. The condition lasted over 35 days in spite of several different treatments, electricity not excepted, and finally a positive result was obtained through injection of 0.5 cc of pituitrin, repeated twice. The author claims a positive action of pituitrin in paresis and other functional disturbances of the bladder and suggests that fresh preparations be used to insure the desired results. Catarrhal and inflammatory conditions of the bladder should previously be treated. Pituitrin is especially efficacious in cases of acute retention due to functional disturbances of the motor apparatus—G V

(HYPOPHYSIS) Specimens from the case of obesity (?), dispituitarism (?), hypernephroma, shown at last meeting. Smith (E B) & Donaldson (R), *Proc Roy Soc Med*, (Lond), 1922, 15, 30

Report of post-mortem findings of a patient who was regarded by Dr Smith as a case of dispituitarism associated with diabetes and as a case of hypernephroma by two of his colleagues. The patient had been admitted to the hospital to see if he would improve on a starvation diet, but instead, no reduction in sugar occurred, and there was an increase in acetone and diacetic acid. He was threatened with diabetic coma and became drowsy, so that he was put back on full diet. For 3 or 4 days he was improved, then convulsions and death occurred. The following were the post-mortem findings. There was an incipient moustache, and the hair had a feminine distribution. On the trunk, at the level of the umbilicus, the fat had a depth of $2\frac{1}{4}$ in. There were multiple small hemorrhages under the skin, the pituitary gland was normal, the pineal gland was small. No thymus could be found, but an enormous pad of fat covered both lungs. The aorta was hypoplastic. The suprarenals were slightly larger than normal, soft and flabby. The pancreas presented areas of necrosis, with areas of fat necrosis about this organ. The testicles were infantile and showed fibrosis with very few interstitial cells and no evidence of spermatazoa formation. A noteworthy feature was the discovery in the transverse mesocolon near the hepatic flexure of a small nodule which was regarded by the observer as an accessory suprarenal. A similar but smaller mass was found near the head of the pancreas—I B

A case of HYPOPHYSEAL tumor treated by radiotherapy (*Un cas de tumeur hypophysaire traitée par la radiothérapie*) Souques,

Mouquin & Walther, III Réunion neurol internat ann, Paris, 1922, abst, Presse méd (Par), 1922, 30, 615

The authors describe a woman of 25 years who has had migraine since she was 11 years old and who has had a hypophyseal tumor for 2 years, revealed by visual hallucinations. There was temporal contraction of one visual field and blindness of the other, with optic neuritis followed by stasis and finally arrest of the menses. The sella turcica was enlarged. Radiotherapy stopped the violent headaches and the amenorrhea, but some degree of adiposity appeared
—R G H

(HYPOPHYSIS) The Mongolian idiot. A preliminary note on the sella turcica findings. Timme (W), Arch Neurol & Psychiat (Chicago), 1921, 5, 568-571

In 23 out of 24 nonselected cases of Mongolian idiocy the radiograph of the skull showed a peculiar change from the normal in the anterior portion of the fossa pituitaria. This change consisted in an excavation of varying degrees under the anterior clinoid processes and presumably under the olivary process and optic groove, and the excavation communicated directly with the anterior portion of the fossa itself. In view of the abnormal bodily and sexual development of Mongolian idiots and of the relation of the hypophysis to development it is suggested that the author's findings point toward an etiological connection. He suggests that careful studies of the hypophysis should be made at all autopsies of Mongolians —R G H

(HYPOPHYSIS) Local asphyxia (Asphyxie locale). Van Temsch, Scalpel (Brux), 1922, 75, 641

A woman of 23 showed local asphyxia of both hands with livid cyanotic color of the fingers and the nails. Pribram has described the effect of hypophysis treatment in Raynaud's disease and the author tried it in this case also with good success —J K

Experimental production of GIGANTISM by feeding anterior lobe of the HYPOPHYSIS. Uhlenhuth (E), J Gen Physiol, 1921, 3, 347-365

Metamorphosed salamanders were fed on a pure diet of anterior lobe of the hypophysis of cattle, controls were fed on earth-worms. The growth of the animals fed on hypophysis was greatly increased over that of normal animals. This growth did not cease after they had reached the normal size of the species, giants being produced. The largest animal of the species *Ambystoma opacum* fed on hypophysis was 19 mm larger and of the species *Ambystoma tigrinum* about 28 mm larger than the largest normal animals of these species known to the author —H A McC

Les troubles visuels dans les syndromes **HYPOPHYSAIRES** Velter, III Réunion neurol internat ann, Paris, 1922, abst Presse méd (Par), 1922, 30, 607

In hypophyseal disorders the ocular symptoms are of great semiologic value because of their frequency, their early development, their therapeutic importance and as true objective criteria of treatment. Statistics of Uthoff show that out of 207 cases of acromegaly there were more than 100 cases of bitemporal hemianopsia, but only 11 cases of papillary stasis. The statistics of Cushing and of Lapersonne are concordant. There are several semipathognomonic symptoms of lesions of the basal region. By far the most important are the changes in the visual field. Bitemporal hemianopsia shows a lesion of the chiasm. Generally the lesions are unequally distributed. The deficit of the temporal fields is not symmetrical. The central vision is usually spared, with the exception of the loss of the macular field. The pupillary troubles are variable. The most common is pupillary inequality with conservation of the light reflex. The hemianoptic reaction of Wernicke is exceptional. A discordance exists between functional troubles and lesions ascertained by the ophthalmoscope, which often does not show anything but decoloration of the papilla on the temporal side. In 15% of the cases papillary stasis exists due to hypertension. Visual acuity is connected with stasis or atrophy. Oculomotor troubles as well as exophthalmos are connected with lesions of the base. It is the chiasmic syndrome which is most characteristic, demands diagnosis and renders especially important radiography of the sella turcica. Radiotherapeutic treatment has often given excellent results upon visual disorders.—R G H

(**HYPOPHYSIS**) Glycosuria in pregnancy Wallis (R L M), Proc Roy Soc Med (Lond), 1922, 15, 31-32

Special attention was directed to the mild type of the condition, rather than to severe glycosuria. Plotting out the curves, they were found identical with those in hyperpituitarism, suggesting that the pituitary plays some rôle in pregnancy.—Physiol Abst, 7, 252

Classification and etiology of INFANTILISM (Ueber Abgrenzung und Entstehungsursachen des Infantilismus) Borchardt, Deutsches Arch f klin Med (Leipz), 1922, 138, 129-143, Deutsche med Wchnschr (Berl.) 1922, 48, 406

Infantilism is a real retarded development, a kind of "subevolutionism," which in growing persons produces a state of mind and body belonging generally to much younger persons. Adults with infantilism have a state of mind and body much less developed than normally. The author proposes a classification as follows: hereditary infantilism, infantilism due to harmful effects on ovum or spermatozoon (alcohol, lead, x-rays), endocrine infantilism (dys-

thyreogeneous, hypophyseal and pluriglandular infantilism), and dystrophic infantilism (from early infection, such as intra-uterine, syphilis, tuberculosis, etc., from defective feeding, from use of alcohol in childhood, and from congenital or early developed heart disease) —J K

Epidemiological and clinical contributions on malarial INFANTILISM (Contributo epidemiologico e clinico sull' infantilismo malarico) Chimisso (L), Riforma med (Napoli), 1922, 38, 241-243

Report of a few cases of malarial infantilism found in Campomarino (Molise-So Italy), a region infested by malaria. The population, originally Albanian, immigrated to Italy about 1460. It is a striking example of degeneration, caused by malaria, of a once tall and powerful race. A big splenic tumor is always found in these cases of real infantilism, and Prof Cardarelli quotes an interesting case in which, after removal of the spleen, the infantilism has been cured —G V

Action of LYMPHATIC gland extract on blood cells (L'azione delle ghiandole linfatiche sulla costituzione morfologica del sangue) Galera, Giorn di Clin med (Parma), 1922, 3, 1-4

The author, bearing in mind the connection between lymphatic glands and white blood elements, and also between these and the loss of virulence of the Koch bacillus in animals, seeks to ascertain whether a similar action is possible on the living blood of man by means of calf gland extract. The glands were reduced to a thin pulp, mixed with an equal part of physiological saline solution and shaken. After about an hour's refrigeration the mixture was passed through a filter and sterilized in an autoclave at 110° C. Injections of 5 cc of extract were made on alternate days in patients suffering from pulmonary or peritoneal tuberculosis. The blood was examined before the injection, and also 4, 24, and 48 hours afterwards. The following approximately constant modifications were seen: leucocytes after 4 hours, increase of 3000 to 4000, less at the 24th hour, and normal at the 48th; eosinophiles and basophiles, without modification in their number; lymphocytes, increase of 10 to 15 at the 4th hour and from the 24th diminution, attaining normality at the 72d; large mononuclears only slightly increased —P M N

Carbohydrate metabolism in diseases of the LIVER (Kohlenhydrat-hydrat-Stoffwechsel der Leberkranken) Hetényi (G), Deutsche med Wchnschr (Berl), 1921, 48, 420

In diseases in which the quantity of parenchyma is decreased the formation of sugar in the liver is decreased also. When the bile passages are obstructed the formation or the fixation of glycogen in the liver is diminished. Diseases of the parenchyma cause a low amount of blood sugar, when the bile passages are obstructed the

blood sugar is often increased. However, in diseases of the parenchyma, compensatory hypertrophy may neutralize its influence. As concomitant lesions of the pancreas may also have a complicating influence the authors conclude that blood sugar determinations have but little value in the diagnosis of diseases of the liver.—J K

Carbohydrate metabolism in diseases of the LIVER (Kohlenhydratstoffwechsel bei Leberkranken) Hétényi (G), Deutsche med Wchnschr (Berl), 1922, 48, 770-771

When 100 gm of glucose are ingested on the empty stomach there is always a rise of blood sugar. This rise is much higher in diseases of the liver than in other diseases. If the rise is not over 40% the liver is probably not diseased. When it is found in healthy persons it is probable that the liver function has suffered from the war. The function of the liver cannot be determined by the alimentary glucosuria for that depends upon the function of the kidneys.—J K

(LIVER) Cardio-vascular effects of hepatic extracts (Les effets cardio-vasculaires des extraits hépatiques) Roger (H), Presse méd (Par), 1922, 30, 441-445

Roger demonstrated the presence in the liver of substances which influence the blood pressure and the heart action in opposite directions. He used intravenously on dogs and rabbits extracts of liver tissue obtained by autolysis, by sulfuric acid and by alkaline (barium) hydrolysis. (The work is a continuation of the experiments with extracts of renal tissues, which were published in the Presse méd, 1918 and 1921.) The concentration, the rapidity of injection, and the method of extraction were found to influence the character of the reactions obtained. In order to abolish the effect of peptones in the extracts, Roger used precipitation with alcohol, with ether or with bichloride of mercury after treatment in vacuo, the residue was taken up saline solution. (Detailed data on the chemical procedures and many tracings on blood pressure and cardiac action are given in the original.) Roger believes that the extracts contain several substances, of which the isolation may prove to be very difficult, as they are likely to be altered or destroyed in the process. He succeeded, however, in isolating a substance which chiefly influences the action of the heart, its effects were studied with the electrocardiograph, and the findings compared with those following injections of atrophine sulfate, while the immobility of the animal was assured by very small amounts of morphine, which, alone, did not affect the heart. The extracts secured by alkaline hydrolysis gave the most interesting results, they produced sinus-bradycardia, and, notwithstanding the constriction of the blood vessels which should have caused hypertension, a marked fall of the blood pressure. Roger believes that some of these substances may play a part, perhaps normally, but especially in cardio-hepatic dis-

turbances, by their introduction into the blood stream in minute amounts following cell destruction, as they occur in extracts obtained by autolysis. He thinks that the alkaline, etherized extracts may prove to be of therapeutic value when the method of extraction has been perfected, because they act selectively on the heart and the blood vessels —G L

The OVARIAN CYCLE and its influence upon uterine changes (*Der Ovarialcyclus und sein Einfluss auf die Veränderungen des Uterus*) Schroder (R), Klin Wchnschr (Berl), 1922 (Feb 25), 1, 403-405

An excellent review, without new facts, of the chronological relationships between the ovarian and uterine changes at the various phases of the menstrual cycle —J K

An accessory PANCREAS in the wall of the gall bladder of a dog Mann (F C), Anat Record (Phila), 1922, 23, 351-353

A small pancreas, located immediately under the serosa of the gall bladder, is described. There was no connection with the major pancreas. Three small ducts emptied directly into the gall bladder. A few definite but very small islands were found in the accessory gland —W J A

An attenuated form of hepato-PANCREATIC cirrhosis with bronze DIABETES (*Une forme atténuée de cirrhose hépato-pancréatique avec diabète bronzé*) Labbé (M) & Stévenin (H), Bull et mém Soc méd des hôp de Par, 1922, 46, 785-788

A report of a mild case of bronze diabetes lasting for two years and terminating by gastric cancer —F S H

Clinical and pathological TETANY (*Beiträge zur Klinik und Pathologie der Tetanie*) Elias (H) & Weiss (S), Wien Arch f innere Med, 1922, 4, 59-64

Elias and Spiegel confirmed their former convictions that in tetany there is an increase in the inorganic and the total phosphorus. When the tetany becomes latent the quantity of phosphorus does not become normal, but for some unknown cause may become even higher —J K

(PARATHYROID) Postoperative TETANY Kaposi, Klin Wchnschr (Berl), 1922, 1, 1334

No details are given —J K

The influence of PARATHYROIDECTOMY on the skeleton of animals normally nourished, and on rickets and osteomalacia produced by deficient diet Korenchevsky (V), J Path & Bacteriol (Cambridge), 1922, 25, 366-392

These experiments were made on 35 rats, from 21 of which the parathyroids had been successfully removed. The remaining 14

served as controls Parathyroidectomy produced no marked effect on the skeleton of rats kept on normal or ricket-producing diets Vitamin A has an important relation to the metabolism of calcium in the organism and particularly in the bones and to the etiology of rickets or osteomalacia The changes typical of rickets or osteomalacia occur most readily and most frequently in rats kept on a diet deficient in both vitamin A and calcium Parathyroidectomy affects the teeth, as shown by Erdheim, but diets deficient in calcium, vitamin A, or in both these factors, also produce apparently analogous changes Rickets was produced in rats provided the age was not greater than 3 to 5 weeks at the beginning of the feeding When the special feeding started at the age of about 2 months, a picture characteristic of late rickets or osteomalacia juvenilis resulted, namely, the changes in proliferating cartilage was not well marked Korenchevsky believes, therefore, that there is no essential distinction between rickets and osteomalacia, the only modifying influence being age —J P S

The importance of the PARATHYROIDS and the treatment of postoperative tetany (*Die Bedeutung der Epithelkörperchen und die Behandlung der postoperativen Tetanie*) Landois (F), *Ztschr f arztl Fortbild* (Jena), 1922, 19, 321-325

A general review For treatment of postoperative tetany parathyroid tablets and calcium lactate up to 30 gr daily are given—when necessary intravenously When possible a graft is made If all the parathyroids are ablated, the author thinks any treatment is absolutely useless —J K

Transplantation of PARATHYROID in general and as a treatment of especially Parkinson's disease (*Über die Verpflanzung der Nebenschilddrüse im allgemeinen und alsbittelgegen Paralysisagitans im besonderen*) Madlener (M), *Zentralbl f Chir* (Leipz), 1922, 49, 703-705

In 16 operations for goiter the author removed small pieces of tissue, which he believed to be parathyroids A real parathyroid was found only 5 times Borchers (*Endocrin*, 5, 375) is right when he states that no transplantation should be made without histological examination Even though the graft does not continue to live, such a transplantation may be extremely useful in cases of temporary parathyroid insufficiency Most grafts are for postoperative tetany, only once has the operation been carried out for Parkinson's disease (Kull) The author performed a transplantation in a man of 52 who suffered for 7 years from paralysis agitans Three days after the operation the rigidity of the muscle was diminished, though the tremors continued After 3 weeks the patient was markedly better, but 6 weeks later all symptoms had returned An unknown quality perhaps exists so that it is of importance to continue trying the graft in other new cases —J K

PARATHYROID coma (Das Parathyreoprive Koma) Melchior (E), Zentralbl f Chir (Leipz), 1922, 49, 667-669

Some time ago Melchior described a form of coma after ablation of the thyroid. He gave the following proofs to the effect that it was due to a loss of parathyroid function. Severe tetany may end in coma. Many years ago Schiff discovered that complete ablation of the thyroid sometimes produced coma and we now know that this would not be caused by a loss of the thyroid itself. Stankovic has described many soldiers (without operation) dying in coma with positive symptoms of Trousseau and Chvostek. In medical literature many unexplainable cases of death in coma after large resections of goiter are described. Mann has described a patient who showed a severe coma after removal of a goiter and ligation of the four arteries. This patient had formerly had epilepsy and a relation between epilepsy and tetany is claimed. The coma after ablation of the thyroid is of parathyroid origin.—J K

Neurotic TETANY due to respiration and the treatment of tetany with ammonium phosphate (Über neurotische Atmungstetanie und über die Behandlung der Tetanie mit Ammonphosphat) Porges (O) & Adlersberg (D), Klin Wchnschr (Berl), 1922, 1, 1200-1201

Vernon was the first author to describe the outbreak of tetany after exaggerated respiration. He examined some patients with very deep breathing, showing tetanic symptoms. Grant and Goldman state that in deep respiration the blood loses CO₂, and shows a more alkaline reaction. In this way the calcium salts become less soluble, thus causing tetany. The best treatment, therefore, is to increase the acidity of the blood. This may be attained by carbohydrate free food, inspiration of air mixed with CO₂, muscular work and administration of ammonium salts of inorganic acids. All of these methods are successful. As a salt of ammonium the phosphate is recommended, since the chloride is not palatable.—J K

TETANIE Porges (O) & Adlersberg (D), Wien klin Wchnschr, 1922, 35, 235-236

Vernon discovered some 10 years ago that persons showed all symptoms of tetany after energetic and slow respiration. Two patients were examined. One a nervous woman with perhaps a tumor of the lungs and of a kidney, began to breathe very hard during a cystoscopy. She developed a typical attack of tetany. The other patient showed an increased respiration during a lumbar puncture and had a tetanic fit also. When the patients respiration was normal they did not show any symptoms of latent tetany. The authors state that during exaggerated respiration the blood loses CO₂ and becomes more alkaline and the calcium of the blood may be partly changed to a less soluble form. In this way respiratory

tetany may also be explained as caused by a decreased calcium content—J K

(PARATHYROID) Tincture of hyoscyamus and hyoscin in Parkinson's disease effect on tremor and sleep (La teinture de jusquiame et l'hyoscine dans la maladie de Parkinson influence sur le tremblement et le sommeil) Rebattu, Mollon et Sédailan, Presse méd (Par), 1922, 30, 241

Rebattu, Mollon and Sédailan reported satisfactory results from the use of tincture of hyoscyamus combined with hyoscin in several cases of Parkinsonia, in athetosis and in chorea (Meeting of the Soc méd des hôp de Lyon) They made the following observations. Injections of hyoscin alone are dangerous and difficult, symptoms of intoxication occurred with 0.5 mg, the effects on tremor and sleep are transient. Administration of hyoscin by mouth (maximum dose, 1 mg) is less dangerous, sleep improves, but the tremor is affected little. The combination of hyoscyamus with hyoscin caused both tremor and pains to disappear entirely for three days in one patient, who also slept much better. Tincture of hyoscyamus alone diminishes the tremor and the pains to a certain extent, causes the patients to sleep better and improves their general condition. Contrary to Erb's observations hyoscin does not seem to be contra-indicated by cardiac lesions, it was used without producing any untoward effects in a patient with mitral insufficiency, and for another patient with a "persistently slow pulse". The authors conclude that, since the combination of tincture of hyoscyamus with hyoscin controls the tremor, abolishes the pain, induces sleep and promotes well-being without untoward effects, this method of treatment offers advantages and should be given a further trial. (The dosage of the tincture of hyoscyamus is not given)

—G L

Histology and physiology of the human PINEAL GLAND (Zur Histologie und Physiologie der menschlichen Zirbeldrüse) Walker (F K), Ztschr f d ges Neurol u Psychiat (Berl & Leipz), 1922, 74, 314-330

The paper deals specifically with the large cells with smooth knob-like process found in the perivascular tissue of the pineal gland. The author concludes that these cells are specific elements and not glia cells nor nerve cells. Hyperplasia of these cells is described in four cases of brain tumor with distinct intracranial pressure. In two cases of congenital hydrocephalus without pressure symptoms this hyperplasia was not in evidence, although in one case the gland was greatly enlarged. He explains the atrophy (one case) or entire absence (two cases) of the pineal gland in congenital hydrocephalus which he found in one year old children with marked pressure symptoms as being due to secondary atrophy produced by the excessive pressure of the cerebrospinal fluid, there

having, in all probability, first been the usual hyperplasia. These observations he thinks strengthen his earlier idea that the pineal gland may act as a reflex center governing the secretion of cerebrospinal fluid and hence intracranial pressure. He hopes to be able to report soon on an abundance of clinical material along this line. Some literature is given.—A. T. R.

Indications for the removal of the SPLEEN in infants and children
Bartlett (F. H.), *Am J Dis Child* (Chicago), 1922, **23**, 283-309

Bartlett collected the reports of all previous splenectomies under 14 years of age, amounting to 51 cases. He adds 3 to the literature. In studying and analyzing the cases reported and his own, he comes to the following conclusions. The conditions for which relief or cure by splenectomy may be indicated are present in the first 5 years of life more frequently than is generally accepted. It is desirable to remove the spleen in the early stages of the pathological process for which splenectomy is indicated. Hemolytic jaundice presents the most favorable condition for splenectomy. Banti's disease and Gaucher's disease represent pathological processes for which splenectomy may give relief of symptoms and may serve to prolong life. Von Jaksch's disease is probably not an independent condition. Indications for the removal of the spleen depend upon certain criteria, not on the making of a definite diagnosis, these criteria are splenomegaly, secondary anemia, and the failure of repeated blood transfusions to determine any improvement in the anemia and general condition.—M. B. G.

A clinical and radiographic study of the THYMUS in infants
Blackfan (K. D.) & Little (K.), *Am J Dis Child* (Chicago), 1921, **22**, 459-471

Sixty patients without symptoms referable to the thymus were examined with particular reference to percussion dulness and to the roentgenray shadow of the thymus. They ranged in age from 5 hours to one year. They regarded the thymus as "negative" if dulness extended not over seven-eighths of an inch to the left, if there was no dulness, or if it was not over half an inch to the right of this point. Dulness in the second interspace both to the right and the left of the midsternal line and continuous with the cardiac dulness below was regarded as a "positive" thymus. Disappearance of dulness with the head in extreme dorsal flexion was confirming evidence. In the "positive" thymus, the x-ray shadow in the anterior mediastinum was either continuous with the heart shadow, obliterating the normal cardiac angles, or it was superimposed on the heart shadow as a broad cap. Thirty-one of the 60 patients failed to show a shadow in the anterior mediastinum, indicative of the thymus. Twenty-nine showed a shadow which was indicative of the thymus. A comparison of the roentgen ray findings and the physical findings show that 27 patients were negative both with the x-ray and on per-

cussion, 20 patients were positive both with roentgen ray and on percussion, 4 were negative with the x-ray and positive with percussion, 9 were positive with the x-ray and negative on percussion. In 6 infants who showed clinical symptoms of enlarged thymus on percussion there was found an increased dullness to the right and left of the midsternal line in the second interspace, which was continuous with the cardiac dullness. In each patient the roentgenogram revealed a shadow in the anterior mediastinum indicative of enlarged thymus. In an analysis of over 200 x-ray pictures it proved impossible to find any points of differentiation between the roentgen ray shadow found in patients with the clinical symptoms of enlarged thymus and the thymus shadow in "normal" infants. They believe that a shadow in the anterior mediastinum which does not show any diminution in size after intensive roentgen ray therapy is not the shadow of the thymus. In case of the doubt roentgen ray treatment should be administered. In one patient it was found that percussion dullness as obtained after death corresponded closely to that during life, that this area of dullness was identical with the shadow cast by the roentgen ray and that the difference of the shadow cast before death and after death was very slight. They felt that the shadows cast in this series should be recognized as due to the thymus since it disappeared after x-ray treatment, it could not be distinguished from the shadow which at necropsy was proven to be cast by the thymus and that it was identical with that found in patients with clinical evidence of enlarged thymus—M B G

(THYMUS) Respiratory obstruction resulting in death. Bruce (J W) & Graves (S). *Am J Dis Child* (Chicago), 1922, 23, 438-441

A case is reported of a boy 4 months of age whose illness dated from the day after his birth when his mother noticed that his breathing was more noisy than normal. This noisy breathing became more and more pronounced. He had been cyanotic only once for about five minutes when he seemed to strangle. Even though physical examination and roentgenograms of the chest showed no abnormality, a diagnosis of enlarged thymus was made and roentgen ray treatment at one week intervals for four weeks was instituted. For 48 hours after each treatment his condition was worse, the stridor becoming more pronounced, the breathing more difficult and cyanosis present. He was not benefited by the x-ray treatment. About one week before his death, his condition became worse, respiratory difficulty and cyanosis being almost constant. Necropsy revealed nothing unusual except malnutrition and an unusual shape and location of the thymus. It was 3 gm in weight, situated 10 mm above the sternoclavicular joint and roughly triangular in shape. No other reason being apparent the authors feel that the enlarged thymus was the cause of death—M B G

The action of soft x-rays upon the **THYMUS** Erlichówna (Marta),
Trav du lab de l'inst M Nencki, 1921, 3, No 1, reprint 23 pp

Soft x-rays ($\frac{1}{2}$ to 2 H) produce in the thymus (rabbit) a somewhat less marked degeneration and cellular destruction than the hard rays (10 to 50 H) The general effects are moderate anemia, loss in body weight, and an increase in the albumin in the blood as determined refractometrically These effects are considered to be due to the poisonous action of the degenerating thymus X-ray therapy has its dangers —Physiol Abst, 1922, 7, 194

THYMUS development (Die Entwicklung der Thymus beim Rind)
Hagstrom (M), Anat Anz (Jena), 1921, 53, 545-566

Of morphological interest only —A T R

(**THYMUS**) Evidence for the existence of lymphatism in suicide cases (Zur Pruffung des Lymphatismus des Selbstmorders)
Hammar (J A), Vrtljschr f gerichtl Med (Berl) 1917, 53 217-236

Data from accurate quantitative analyses of the thymus in 18 cases of suicide between 17 and 35 years of age were compared with similar determinations on the thymus of 17 accident cases from 16 to 35 years of age, there was found no morphological evidence for the idea that the thymic parenchyma is supranormal in amount in suicide cases Neither the whole thymus, cortex, medulla nor proportion of cortex to medulla ("index") was larger in the cases of suicide than in the accident cases with sudden death In 5 out of the 18 suicide cases the parenchyma was below the lowest found in any accident case Hassall's corpuscles were irregular In 11 suicide cases the absolute and the relative number of corpuscles were less than the average of the accident cases and in 6 cases even less than the smallest number found in the accident cases —A T R

Further elucidation of the structure of the **THYMUS** in so-called thymic death microscopical analysis of the thymus in 24 cases of mostly sudden death from internal causes (Zur fernerren Beleuchtung der Thymusstruktur beim sogen Thymustod mikroskopische Analyse der Thymus in 24 Fallen meistens plotzlichen Todes aus inneren Grunden) Hammar (J A), Ztschr f Kinderh (Berl), 1917, 15, 225-312

An exhaustive quantitative analysis of these thymi gave no evidence of any abnormality beyond that seen in cases which have met accidental death from external causes Medullary hyperplasia was no more frequent in cases diagnosed as "thymic death" than in accident cases of similar age The thymus seemed in no way to have been involved as a factor which could cause death The cause of death in these cases, he thinks, must evidently be looked for elsewhere, mostly likely in other organs of internal secretion

—A T R

Microscopical analysis of the THYMUS in 25 cases of acute infectious diseases (acute anterior poliomyelitis, scarlatina, measles, whooping-cough, typhoid fever and in one case each of starvation and snake bite) [Verhalten der Thymus bei akuten Infektionen mikroskopische Analyse der Thymus in 25 Fällen von akuten Infektionskrankheiten (Poliomyelitis anterior acuta, scarlatina, morbilli, pertussis, typhus abdominalis) Als Anhang Die Thymus bei einem Todesfall durch Hunger und einen durch Schlangenbiss] Hammar (J A) Ztschr f ang Anat [etc] (Berl), 1918, 4, 1-107

A very detailed quantitative analysis with the following results Poliomyelitis (11 cases) presented a thymus variable in size but generally within normal limits, but invariably with an absolute and relative increase in the number of small Hassall's corpuscles. A few cases showed more or less accidental involution. The 9 cases of scarlatina were characterized by marked accidental involution with a large increase in the number of small Hassall's corpuscles. The 3 cases of measles and single case of pertussis showed also marked involution and numerous small corpuscles. The parenchyma of the thymus in the typhoid fever case was distinctly subnormal in amount, but large Hassall's corpuscles were overabundant. The starvation case (due to congenital pyloric stenosis) agreed well with experimental inanition effects on the thymus, there being reduced parenchyma and high relative but low absolute number of Hassall's corpuscles. In the case of the snake bite the picture was essentially like that in most of the above acute infections (marked involution and increase in small corpuscles), except that there was more calcification. Graphs, literature, etc., are given—A T R

Microscopic analysis of the THYMUS in a number of cases of congenital lues (Beitrage zur Konstitutionsanatomie VII Mikroskopische Analyse der Thymus in einigen Fällen von Lues congenita) Hammar (J A), Beitr z path Anat u z allg Path (Jena), 1919, 66, 37-91, 195-258

This paper deals with the detailed quantitative histological examination of the thymus in 11 cases of congenital lues and one questionable case. As a direct result of the syphilitic infection the author found one case with a Dubois abscess and in all cases a high degree of lymphocytic infiltration of Hassall's corpuscles, but these changes are not considered entirely differential for congenital lues. Hypoplasia and accidental involution are considered indirect results of syphilis. An increase in connective tissue, thickening of the adventitia of blood vessels and the presence of "epithelioid" cells are not considered organ changes that are specific for congenital lues. Extensive literature is reported—A T R

Microscopical analysis of the THYMUS in 25 cases of Graves' disease (Beitrage zur Konstitutionsanatomie I Mikroskopische

Analyse der Thymus in 25 Fällen Basedow'scher Krankheit)
Hammar (J A), Beitr z klin Chir (Tübing), 1917, 104,
469-614

In 18 cases of Graves' disease the thymi were found to have a supranormal amount of parenchyma, in 7 cases the parenchyma was normal or subnormal. In all cases where the total weight of the gland was above the normal, the parenchyma was supranormal and it was so in 4 cases where the total weight fell within the limits of normal variation. When hyperplasia of the thymus took place the cortex was always involved. The medulla was supranormal in some cases, but not in all. Where both cortex and medulla are supranormal the cortex exhibits the greater increase. There is always an increase in the number of Hassall's corpuscles, both in the total number and in the number per mg of parenchyma. The smaller corpuscles are especially plentiful and calcified corpuscles are almost entirely lacking. These conditions are found also in the thymi which show a normal or subnormal amount of parenchyma. The small size of these last is probably due to an accidental involution. Since the thymi in Graves' disease do not resemble those of the infantile type nor those found in cases of thymic death or "status lymphaticus" the author concludes it is more accurate to call the condition one of hyperplasia than of subinvolution, persistence or revivescence. The enlargement of the parenchyma seen in these cases was not unlike that found in other conditions, but the number and kind of Hassall's corpuscles are peculiar to Graves' disease. The organs were studied by the projection method used by the author in earlier work on the thymus. A greater accuracy in measuring the total amount of parenchyma and the relative amounts of cortex and medulla is secured by this method. The use of other methods, such as measuring by eye, has led to the frequent reports of medullary hyperplasia in Graves' disease. Another source of error has been eliminated in this work by comparing each gland with a number of thymi of the same age, instead of using the infantile thymus as the norm —M M H

A contribution to the topographic anatomy of the THYMUS gland with particular reference to its changes at birth and in the period of the new-born. Noback (G J), Am J Dis Child (Chicago), 1921, 22, 120-145

The thymus was studied in the cadavers of 65 fetuses and full term children by means of dissection, graphic reconstructions and freehand sections. No material was used in which pathological conditions were macroscopically observable. The lobation of the thymus is determined early in fetal life and the establishment of respiration obviously has no effect on it. The thymus in the late fetus and in the new-born is predominantly of the cervicothoracic type. The thymus in the late fetus and stillborn child has a typical

form and quite constant relations. Its lateral surfaces are convex and bulge against the medial surfaces of the lungs. The lungs very rarely extend at all on its anterior surface, and the thymus very rarely extends at all on the anterior surface of the right ventricle of the heart. The thymus in liveborn infants has typical form and relations which are similar to those found in young children. It is elongated and molded so that its anterior, lateral and posterior surfaces bear the impress of all the organs with which it is in contact. Its lateral surfaces usually show marked convexities which are occupied by its lungs which pass over the anterior surface of this organ. Unlike the fetal thymus, it usually extends more inferiorly passing over the right ventricle. The change from the broad or fetal type of thymus to the elongated and molded type found in the liveborn bears a direct relation to the establishment of respiration and is dependent on the expansion of the lungs. The organ is compressed from side to side by the medial surfaces of the expanding lungs. It is compressed anteroposteriorly by the anterior borders of the lungs which become more thickened early in the establishment of respiration as they gradually overlap the thymus—M B G

X-ray treatment of the THYMUS in psoriasis (*Zur Thymusrontgenbestrahlung bei Psoriasis*) Schneider (P), Wien klin Wchnschr, 1922, 35, 565-566

Brock has advocated the treatment of psoriasis by x-ray treatment of the thymus. Schneider tried this treatment in 12 cases and a good effect was seen only twice. It has not yet been proved that there is a relation between the thymus and psoriasis—J K

Epitheliomata of THYMIC origin Symmers (D) & Vance (B M), Arch Int Med (Chicago), 1921, 28, 239-251

Only three examples of primary thymic epithelioma are to be found in the literature. A fourth is recorded in this paper. The lymphocytic tumors far outnumber the epithelial and occur usually at a younger age. Intrathoracic pressure signs are inconstant, in some cases negligible, in others very severe and quite sudden in onset. Lymphosarcoma of the thymus, as elsewhere, invades adjacent tissue, but metastasis is apt to be a late event. The lymphoid growths should be benefited by the roentgen ray—H L

THYMUS apoplexy An unusual manifestation of hemorrhagic disease of the newly born. Wahl (R N) & Walthall (D), Am J Dis Child (Chicago), 1922, 24, 27-44

Because of the rich blood supply, the thymus is apt to become congested, especially whenever there is general circulatory stasis. Hemorrhage may be scattered, small and petechial in character or it may appear as large effusions of blood localized or diffused throughout the substance of the organ. The former are common, especially

In asphyxial conditions in acute infections and in hemorrhagic diseases. The latter, to which Friedleben gave the name of "Apoplexien" are relatively rare. Such an "apoplexy" may follow hyperemia associated with simple hyperplasia of the gland and may give the appearance of a hemorrhagic infarct. They usually occur in very young infants or the new born and are often associated with sudden death. The etiology of the condition is obscure but seems to be associated with syphilis more than with any other factor. Circulatory stasis, trauma, nonspecific infections and hemorrhagic tendency are contributing, if not the main factors in some cases. There is no way of making a clinical diagnosis. The authors analyse the 19 cases in the literature and add two of their own. Their cases occurred in children 4 days and 6 weeks old, respectively. Both showed symptoms of meningeal irritation, lateral nystagmus, generalized icterus, marked increase in the coagulation time of the blood, and hemorrhage. Labor, while not normal, was not unduly difficult or prolonged in either case. In each case, the necropsy findings showed a cerebral hemorrhage, inflammatory changes in the lungs suggestive of syphilis and a diffuse hemorrhagic infiltration of the thymus in which the extravasation of blood was both intra-lobular and interlobular and was associated with suppuration, necrosis and marked proliferation of the reticular epithelial cells.

—M B G

The chemical composition of the THYMUS and the relation by weight between this organ and the THYROID (*Recherches sur la composition chimique du thymus et sur les rapports pondéraux entre cet organe et le corps thyroïde*) Zunz (E), Arch intern de physiol (Liège & Par), 1920, 15, 459-472

It is exceptional to observe considerable atrophy of the thymus in the healthy adult man (soldier killed in war). The average weight of the thymus in man from 19 to 34 years is 15 to 16 gm. The maximum surpasses 30 gm. In spite of great individual variation, the percentage of material extracted by ether tends to increase with age. The weight of the whole fresh thymus which has been extracted by ether and then dried tends to be increased more when the weight of the thyroid is less. It is always less than that of the thyroid gland when the latter weighs more than 29 gm. in the fresh state. It is greater than that each time the thyroid weighs less than 19 gm. The content of the thymus gland, the dry residue, the nitrogen, the phosphorus and the ash does not appear to have any relation whatever to the age of the subject, to the weight of the fresh thymus or to the weight of the thyroid gland. The chemical composition of the thymus among healthy adults is relatively constant. The phosphorus lipid of the thymus is relatively constant, but the quantity present is not great.—Physiol Abst 6, 71

(**THYROID**) Substances with specific action prepared from single organs IV (Studien über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung IV) Abderhalden (E) & Schiffmann (Olga), Arch f d ges Physiol (Berl), 1920, 183, 197-209

The corresponding effects of (a) fresh normal human thyroid, (b) cattle thyroids hydrolysed by sulphuric acid, the hydrolysate evaporated to dryness, extracted with absolute alcohol, and the extract evaporated under diminished pressure, the residue being dissolved in 100 times its volume of water, (c) the aqueous preparation corresponding to (b) soluble in dilute alcohol, and (d) the corresponding aqueous solution of the residue insoluble in dilute alcohol, were tested on tadpoles of *Rana temporaria* and *Bufo viridis*. The effects of all four were similar in kind, (c) being stronger, (b) and (d) weaker than (a). The most marked effect is on the intestine. The shortening takes place more rapidly, clumps of degenerated epithelial cells are more noticeable, its metamorphosis begins earlier. The growth of the pituitary is lessened. No very definite results were obtained on the thyroid and thymus.—A T C

(**THYROID**) Studies on substances with specific action prepared from single organs VIII (Studien über die von einzelnen Organen hervorgebrachten Substanzen mit spezifischer Wirkung VIII) Abderhalden (E) & Schiffmann (Olga), Arch f d ges Physiol (Berl), 1922, 195, 167-198

When toad-tadpoles of differing ages are treated with fresh thyroid, the younger animals show the growth-inhibition and metamorphosis acceleration more slowly, become more deformed and die before the end of metamorphosis. Older animals react more rapidly and show the effect of thyroid typically. Colloid and exophthalmic goitres produce no, or but slight, action on toad-tadpoles. Thyroids hydrolysed with sulphuric acid act on them but weakly, but have a typical action on *Rana temporaria* tadpoles. Di-iodo-tyrosine and di-iodo-tyramine act on *Bufo* and on *Rana* in the same way as thyroid. The earlier the treatment the stronger is the action. Glycyl-di-iodo-tyrosine, and di-iodo-tyrosine methyl ester produce the same action as di-iodo-tyrosine. Iodo-acetyl-di-iodo-tyrosine, β -iodo-propionic acid, alival, and tyrosine are without action.—A T C

Nocturnal (paroxysmal) dyspnea its treatment with **THYROID** gland Adams (R D), J Am M Ass (Chicago), 1922, 78, 1876-1877

The discussion is confined to those cases in which the cardiovascular system dominates the picture, as myocarditis, aortic disease and arteriosclerosis. The cause of these attacks is discussed. By treating with thyroid gland 15 patients averaging 52 years of age, 12 were distinctly relieved, 2 were unaffected and 1 was un-

favorably influenced The relief following the administration of iodides may be due to thyroid stimulation—W M A

(THYROID) Nutritional needs in myxedema (Der Nahrungsbedarf beim Myxodem) Ambrozic (M), Ztschr f Kinderh (Berl), 1921, 20, 117-126

In studies of nutrition of children with myxedema, thyroidin therapy was used and the conditions found are expressed in terms of v Pirquet's formula The demand during periods when thyroidin was withheld amounted to between 30 and 40 "centinemsiqua", during periods of thyroidin therapy it was always higher, varying between 40 and 67 cnsq, with limits of 37 to 98 cnsq The thyroidin therapy in average doses increased the demand about 15 to 20 cnsq, larger amounts gave a correspondingly great difference

—Chem Abst, 16, 739

THYROID and parathyroids in animals kept in the light or in the dark (Schilddruse und Epithelkörperchen bei Licht und Dunkel-tieren) Aschoff, Munchen med Wchnschr, 1922, 69, 874

No details are given—J K

(THYROID) Radiotherapy in Graves' disease (La radiothérapie dans la maladie de Basedow) Barjon (F), J de méd de Lyon, 1921, abst, Arch méd belges (Brux), 1922, 75, 208

Radiotherapeutic treatment of Graves' disease is beginning to be used in the practice of medicine The results obtained justify its use while at the same time they confirm the toxic origin of the symptoms, due to an abnormal ("anarchic") secretion of the thyroid gland Four very different observations show the rapid action of irradiation upon the toxic symptoms, upon the general nutrition and upon hyperexcitation of the nerves The action is constant and progressive upon tachycardia, but slower and less apparent upon exophthalmic goiter and tremor This treatment is especially adapted to the serious and hypertoxic forms with menacing "subastystolic" symptoms—R G H

(THYROID) Radiotherapy in the treatment of Basedow's disease (Traitement radiothérapique de la maladie de Basedow) Belot (J), Bull méd (Par), 1920, 34, 1063-1066

The author assumes that hyperthyroidism is the main factor in the etiology and symptomatology of Basedow's disease, and therefore concludes that the rational treatment of this affection must be a method which reduces and modifies the thyroid secretion Since the thyroid cells are highly sensitive to x-rays and thyroid intoxication is lessened thereby, this would seem to be the therapy of choice, there is no scar produced and relapses are less frequent than after surgery The early results of x-ray treatments are a reduction of

nervousness, improvement in sleep and in gastro-intestinal symptoms, and in improvement in weight, hyperidrosis, and general well being. The circulatory symptoms, subjective and objective, are ameliorated. The pulse rate descends to 80, but rarely to normal. The goiter itself does not respond so readily, its reduction in size occurs some time after circulatory improvement is evident. Exophthalmos persists to the last, and if pronounced, may never disappear. Irradiation must not be continued because of the persistence of goiter and exophthalmos, lest myxedema result. Penetrating rays properly filtered, the use of a standard Coolidge tube with a 22 cm spark, filtered through 5 to 7 mm of aluminum, are the essentials of technique. The thyroid region is divided into three segments, corresponding to the two lobes and a median region which includes the thymus. The two lateral lobes are treated, this is followed within 4 or 5 days by treatment of the median thyroid region, including the thymus, the dosage being approximately 4 H units. This is repeated every 10 or 12 days upon each segment. Belot emphasizes the importance of individualization in treatment, as a standard technique may not correspond with the requirements of a given case. Properly employed technique need not even discolor the skin. The subcutaneous adhesions complained of by surgeons as due to x-ray therapy are really evidences of improvement of the disease. Cure may be assumed when for two years the general condition has been good with the pulse rate about 80. Of 45 patients treated by the author 20% showed "partial improvement," 70% presented "distinct prolonged improvement," 5% were not improved, and 5% of patients abandoned treatment. In discussing the indication for x-ray therapy, Belot divides his patients into 4 groups. Group 1 comprises patients presenting clear-cut symptoms of the Graves-Basedow type. Radiotherapy is capable of curing 80% of these. Group 2 includes the forme fruste type in which radiotherapy produces very prompt results. Group 3 includes the so-called "Basedowides" of Stern, in which radiotherapy is still a measure under discussion. Group 4 embraces the so-called "secondary Basedow" or toxic adenomata which do not respond to radiotherapy, but should be operated upon.—I B

(THYROID) Transitory paralysis of the recurrent nerve after goiter operations (*Les paralysies transitoires du récurrent après les opérations pour goîtres*) Bérard (L), Lyon chirurg, 1922, 19, 1, abst, Arch méd belges (Brux), 1922, 75, 433

The pathogenic elements of transitory paralysis of the recurrent nerve occur in the following order of frequency. There are twitchings of the lower vascular pedicle and of the recurrent nerve in the act of dislocation without injury of the descending lobe of the goiter which has been called the delivery of the goiter. There may be lesion of the nerve, from careless ligation of the thyroid artery

Finally, and more rarely, there are cicatricial contractions of the tissues at the level of the hemostatic sutures in the vicinity of the recurrent nerves, or the blocking of one or two nerve trunks on account of the serum exuded from the thyroid stump, or by a neighboring hemorrhage. Before deciding upon the transitory character of postoperative recurrent paralysis each stage of the convalescence should be controlled by laryngoscopic examination, since there have been a number of cases of paralysis caused by section of the nerve with a definite cadaveric position of the corresponding vocal cord which seems to be wounded spontaneously, although it is a matter simply of a vocal adaptation by a more pronounced displacement of the healthy cord toward the median line — R G H

(**THYROID**) Does metastatic goiter exist (*Le goître métastatique existe-t-il*)? Bérard & Dunet, *Rev de chir (Par)*, 1921, 59, 521, abst, *Arch méd belges (Brux)*, 1922, 75, 223

The authors deny the existence of benign metastatic goiter, introduced into thyroid pathology by Conheim who described as benign a tumor which Wollfler affirmed to be malignant. That erroneous notion persisted due to the publication of observations on benign goiter, although in the great majority of cases either there was no microscopic examination of the goiter itself or it was made in a very inadequate fashion. Metastatic goiter, so-called benign is a malignant goiter and the thyroid gland does not escape the general laws which govern the development of tumors, malignant thyroid neoplasm alone gives origin to metastases. In the presence of a tumor which is usually osseous, the microscopic examination of which reveals the thyroid nature, it is immediately necessary to investigate the changes which the thyroid gland itself may show. The presence of a large goiter or of even a simple adenomatous nucleus, clinically benign is frequent. But while a secondary tumor exists the clinical absence of signs of malignancy do not permit affirmation of the benignity of the thyroid lesion. Histologic examination may settle the question if made in serial sections and upon the whole initial neoplasm. In this case the microscope sometimes shows truly microscopical points of neoplastic degeneration. The idea of benign metastatic goiter should be eliminated entirely from the list of benign thyroid tumors and should give place to the conception of latent thyroid metastatic cancer — R G H

The morbid anatomy of the **THYROID** in six cases of **DIABETES mellitus** (*En undersökning av Glandula thyreoidica i 6 fall af Diabetes Mellitus*) Bergstrand (H) *Hygiea (Stockholm)*, 1922, 84, 481-493

Bergstrand has examined the thyroid gland of six patients dying from diabetes mellitus. In three the glands were practically normal. In the others the alveoli were irregular in shape and size

The colloid was markedly diminished throughout the glands. The cuboidal epithelium showed some desquamation. In addition two of the glands showed chronic interstitial thyroiditis —D J G

HYPOTHYROIDISM (Über Hypothyroidie) Bolten (G C),
Deutsche Ztschr f Nervenhe (Leipz), 1917, 57, 119-159

A discussion of the function of the thyroid gland with special reference to what the author considers to be a particular form of hypothyroidism described in 1899 by E Hertoghe as "benign chronic hypothyreoidea," but which, according to Bolten, has received far less attention than it deserves. Eleven cases are given to illustrate the various symptoms, which are discussed in detail. He gives the following outline of the symptoms in the adult. There is the primary or direct syndrome, which includes simple hyposecretion or hypofermentation of the stomach and intestine (nervous dyspepsia), metabolic disturbances in the form of incomplete catabolism, hypoecretion of certain salts and delayed metabolism (a form of gout, gouty diathesis, ischialgia, etc., general constitutional obesity, and Dercum's disease), and toxic symptoms, probably resulting from incomplete fermentation during intermediate stages of metabolism, such as genuine migraine (thyrogenic), genuine epilepsy (thyro-parathyrogenic), nervous disturbances of neurasthenic type, psychic disturbances resembling mild dementia praecox, and climacteric disturbances. Then there is the secondary or indirect syndrome (hypotonus of the sympathetic nervous system), which includes trophic and circulatory disturbances of the skin, nails and subcutaneous tissue (form of Raynaud's disease, herpes gangraenosus, etc.), circumscribed edema of the skin, and diminished or increased regenerative power of the skin. Forty references are given —A T R

(THYROID) Prevention of sporadic simple goiter Bram (I),
Internat Clin (Phila), 1922, 2, 109-114

In this illustrated article, the author emphasizes the importance of the clinical differentiation between endemic and sporadic simple goiter through an analysis of etiological factors, with special reference to the presence or absence of geographical conditions. It is easy enough, in a non-goitrous district, to conclude that a given goiter is sporadic in nature. It is rather difficult and often impossible, to make the distinction in patients residing in goitrous districts, as to whether the thyroid enlargement is induced by geographical conditions or otherwise. The writer's clinical observations in a large series of cases indicate this discrimination to be a guide in prophylaxis and treatment. Endemic goiter, a condition resulting from a geographical deficiency of iodine, is successfully managed by iodine administration. Not so with sporadic goiter, the etiology of which is complicated, depending upon excessive demands for thyroid hormone by physiological and pathological conditions elsewhere.

in the body, the organ, incapable of supplying this excess, must hypertrophy in efforts at adjustment. Prophylaxis of sporadic goiter consists in the prevention of tangible causes which are usually referable to the sexual apparatus, or to local or general infection. Pre-natal care of the child by attention to the goitrous mother is suggested in the prevention of congenital goiter. The necessary dietetic and hygienic precautions, the avoidance of excessive physical and mental exertion, and complete rest in bed for two or three days during each menstrual period will often prevent the occurrence of goiter in susceptible individuals. Though iodine administration in endemic goiter is productive of satisfactory results, endeavors to prevent or treat sporadic goiter routinely with iodine yields only occasional success. In a percentage of instances, the goiter becomes larger and toxic symptoms are induced. The drug to be employed in sporadic simple goiter (when a drug is indicated), is thyroid extract, carefully administered. Though iodine is an essential ingredient in all potent thyroid products, it is iodine in its thyroid environment or thyroid in its iodine environment that is required when the thyroid apparatus is to be relieved of its surplus burden of function. Thyroid minus iodine is impotent, with iodine it is thyroid as we know it—a substance at once a blessing and a curse in therapeutics and in sporadic goiter, depending upon whether it is used or abused.

—Author's Abst

The position of the THYROID gland in the endocrine system Brown (W L), Brit M J (Lond), 1922, 1, 85-88

After calling attention to the development of endocrinology and the relation of the autonomic nervous system to the endocrine glands, Brown discusses at some length the various thyroid disturbances. He divides the hyperthyroid cases into three groups, viz, (1) nutritional, (2) toxic, (3) psychic. The author notes the marked influence of the dysfunctioning thyroid on carbohydrate metabolism. The cardiovascular complications of thyroid disease are briefly described. Brown suggests that the parathyroids work with the pancreas and antagonize the thyroid gland. He believes that the thyroid gland should be considered as the activator of the metabolism, it co-operates with the sympathetic system and through it plays an important part in internal and external defense, it mobilizes blood sugar and prevents its escape by raising the kidney threshold, it interacts with the gonads, especially during their retrogressive changes.—F C P

HYPERTHYROIDISM in children before puberty Report of case Buford (R K), J Am M Ass (Chicago), 1922, 78, 1533-1534

The author finds only 18 cases of hyperthyroidism in children under twelve years of age in the literature of the past twenty years. Two have had surgical treatment. The author's patient was 6 years old, showed no improvement after tonsillectomy and medical care.

but was in perfect health one year after partial thyroidectomy
—W M A

The effect of **THYROID** feeding on rats on a vitamin-deficient diet
Cameron (A T) & Moore (A), Tr Roy Soc Canada, 1921, **15**,
29-36

Experiments on pigeons yielded no definite conclusions. It was doubtful if the onset of a definite polyneuritis was accelerated. Decrease in growth-rate in young rats due to thyroid and to deficient diet is additive. No definite conclusions could be drawn as to the joint effect on organ hypertrophy. The thyroid does not enter into a resting condition, as is the case when thyroid is fed with a normal diet —A T C

Case of recurring **THYROIDITIS** without other disturbances. Carling
(E R), Proc Roy Soc Med (Lond), 1922, **15**, 30

The patient was a girl of 7 suffering with an enlarged thyroid in which there were 4 especially hard masses. No other abnormality was detected, and the swelling of the gland subsided spontaneously. The condition recurred on 3 subsequent occasions, at 3 months' intervals. In each instance, spontaneous recovery occurred —I B

Influence of **THYROID** and **ADRENAL** on growth (*Influenza delle glandole tiroide e surrenale sull' accrescimento corporeo*). Castaldi (L), Sperimentale Arch di biol (Firenze), 1922, **76**, 110-113

From extensive histological and biometrical investigations Castaldi concludes that the adrenals play an important rôle in conditioning somatic development. The correlation coefficient was found higher for the cortex than the medulla of the gland, as regards body weight and as regards sexual development the medullary coefficient was least. Hormone factors conditioning both pre- and post-natal growth are involved in a highly complicated way. In the treatment of growth disorders, therefore, pluriglandular preparations, including adrenal cortex, should be used —P M N

THYROID operations in the treatment of exophthalmic goiter (*Les opérations thyroïdiennes dans le traitement du goitre exophtalmique*). Cauchon (A), Bull méd (Par), 1920, **34**, 1060-1063

In France, surgical intervention in Graves' disease is not considered until non-surgical means have been tried without avail, since medical treatment has yielded cure, even in advanced cases. Surgery is especially contra-indicated during the acute phase in the progress of the disease, when there are observed hyperlymphocytosis, high basal metabolism, exaggerated nervousness, cardiac dilatation, marked emaciation, vomiting and diarrhoea. Nonsurgical treatment, especially rest and a rigid hygienic and dietetic regime, should be re-

sorted to, later, the critical stage having been passed, the question of surgical intervention may be faced. In grave cases, or when associated with an enlarged thyroid and there is a hypertrophied thymus, x-ray treatment may be advised. This should not be continued if clearly evident results are not quickly obtained. X-ray treatment should not be continued for a long time in any event, as fibrosis of the gland may render operation more difficult, and in some instances, prolonged irradiation may completely destroy the thyroid, resulting in myxedema. When surgery is to be resorted to, due care must be given the matter of the preparation of the patient. These subjects are extremely impressionable, irritable and sensitive. Each emotional tension exaggerates the syndrome and each fear increases the intoxication of the patient and the risk of operation. The principles of Crile's method of anoci-association are advocated. The author concludes his article with a review of the common operative procedures pursued in representative American clinics.—I B

The cerebrum and **THYROID** function (Il cervello e la funzione tiroidea) Ceni (C), Riv sper di freniat (Reggio-Emilia), 1920, 44, 243-286

In tortoises removal of one cerebral hemisphere produces no apparent change in the thyroid but in birds and also in a certain number of the dogs experimented upon a thyroid hypertrophy occurred as a result of the operation. It is suggested that, in general, vertebrates possess an inhibitory center for the thyroid in the fore-brain.—Physiol Abst, 6, 326

(**THYROID**) Factitious toxicity of previously simple goiter. Chapman (T L), Minnesota Med (St Paul), 1921 4, 148-151

Chapman warns against the indiscriminate use of iodine in the treatment of goiter. The prevention and cure of adolescent and pre-adolescent types of goiter by iodine is an assured fact, but goiter persisting after adolescence, though apparently nontoxic may contain the essentials of toxicity. This may be due to scattered, relatively small areas of hyperfunctioning tissue within the struma, usually of insufficient size and bulk to produce a toxicity sufficient to give rise to clinical symptoms of recognized type. It is also possible that the small excess of thyroid hormones thus formed is neutralized by the protective forces of the body. Iodine may cause symptomless goiters to become toxic, and already toxic goiters to become more toxic. Toxicity caused by iodine administration is therefore a danger to be remembered. These instances of factitious toxicity are cases of thyrotoxicosis. Lastly, Chapman states that iodine administration shortens the period from nontoxicity to toxicity of simple goiter. Generally, a female of 16 to 30 who had sought treatment to improve her cosmetic appearance and had been placed upon prolonged iodine treatment, appears in the clinic because of increasing symptoms, especially goiter tachycardia sweating hands tremor and

nervousness Examination of these goiters proves them to be granular, the cellular elements are confined to small areas, which are typically hyperplastic, though the entire gland never presents the picture seen in true Graves' disease nor do the subjects show true exophthalmos—I B

(**THYROID**) Medical treatment of exophthalmic goiter (*Traitement médical du goitre exophtalmique*) Coulaud (E), *Bull méd (Par)*, 1920, 34, 1066-1069

There are three classes of substances employed by the internist in the treatment of exophthalmic goiter (1) Those not including opotherapy, (2) opotherapy, (3) serums of thyroidectomized animals or thyrotoxic serums Cases evidently of infectious origin are treated along etiological lines Those following acute rheumatic fever are relieved by sodium salicylate Cases of syphilitic origin respond to mercury and arsenic Since the thyroid is rich in arsenic and iodine, these drugs, employed indiscriminately, are apt to produce symptoms similar to those observed when thyroid material is administered Iodine holds little, if any, place in the treatment of this disease Many drugs may be employed for the symptomatic treatment of the disease For the thyroid enlargement, quinine, ergot, and calcium chloride are useful For the insomnia and trembling, the usual nerve sedatives are useful Cardiac symptoms are not overcome by digitalis unless in myocardial insufficiency Ordinarily, tincture of strophanthus in doses of 8 to 10 drops daily is advocated Hydrotherapy also is of value In instances in which the thymus largely participates in the toxic process, opotherapy may be considered Few cases are ameliorated by thyroid opotherapy, these, as pointed out by Gauthier de Charolles, consist mainly of "Basedowified" types of the disease and those cases tending toward myxedema Thyroid opotherapy and iodine administration are alike in their tendency occasionally to relieve but usually to injure patients with exophthalmic goiter Thymus opotherapy, too, has its advocates and its opponents In the author's opinion, thymus gland has been of little, if any, use, and in many instances it is as harmful as thyroid extract Since there is a direct relationship between the thyroid and the genital organs and since there are strong evidences of ovarian insufficiency in patients suffering with exophthalmic goiter, ovarian opotherapy would seem to be a rational procedure A large number of instances of clinical improvement has been observed following ovarian opotherapy while not an instance of an exaggeration of the syndrome has occurred under this treatment By analogy, testicular opotherapy has been employed in men with asserted favorable results, but hardly comparable to the effects obtained in women through ovarian administration Pituitary and suprarenal opotherapy have been employed for their vasoconstricting action Experiments on rabbits with the last mentioned substances have resulted in a diminution of colloid in the thyroid Parathyroid

opotherapy has been recommended, but not upon substantial grounds Revilliet has recommended biliary opotherapy to slow the pulse, but favorable results are not yet forthcoming In concluding his remarks upon opotherapy, Coulaud is of the opinion that this mode of treatment has not given the hoped for results in the treatment of exophthalmic goiter, cures have been extremely rare The hypothesis that following a thyroidectomy there forms in the organism a secretion capable of neutralizing the thyroid substance has led to the use of various serums The blood of the thyroidectomized dog or horse administered to a subject of exophthalmic goiter may improve the tremor, tachycardia, and exophthalmos The blood of a myxedematous person is said to possess analogous properties The desiccated blood of thyroidectomized animals has also been used Moebius' serum is an example Some prefer to use the milk of thyroidectomized goats These substances, when observed to alleviate the syndrome, do so only during the time of their administration On the other hand, they are capable of harm Rogers and Beebe have reported good results from the use of thyrotoxic serum, but subsequently have concluded that treatment is of little, if any, value—I B

(THYROID) The influence of the diet during the war on Graves' disease (*Einwirkung der Kriegskost auf die Basedowsche Krankheit*) Curschmann (H), *Klin Wchnschr* (Berl), 1922, 1, 1296-1298

It is certain that underfeeding influences the thyroid Oberndorfer found at post-mortem examination in all cases of "Hunger-oedem" an atrophic thyroid During the war Curschmann observed a largely increased number of patients with hypothyroidism and with classical myxedema Meat, fat and, in general, a diet very rich in calories stimulates the thyroid and has a bad influence upon the symptoms not only in diabetes, but also in Graves' disease During the war the number of patients with Graves' disease was exceedingly diminished—J K

(THYROID) Malformation deformities of the neck, congenital cysts and fistulae (*Deformità del collo per malformazioni embrionali Cisti e fistole congenite*) De Gaetona (L), *Arch ital di chir*, 1921, 4, 265, abst, *Med Sc* (Lond), 1922, 6, 29

The article includes a discussion of thyroid, parathyroid and thymus tumors It is of technical interest to surgeons—R G H

(THYROID) The value to the surgeon of the basal metabolic rate in toxic goitre Else (J E), *Northwest Med* (Seattle), 1922, 21, 108-116

The basal metabolic rate is an indispensable index of the activity of the thyroid gland An increase in the secretion of thyroxin

is followed by an early rise in the rate, usually before the clinical symptoms are manifest. The height of the rate is not as important as the change in the rate, whether rapidly rising, stationary or falling. Frequent determinations are advisable. A normal or sub-normal rate after an attack of thyrotoxicosis, accompanied by symptoms of the disease is indicative of permanent injury. Such symptoms may persist for life, even though there is no longer an excessive secretion of thyroxin. The prognosis is always guarded with a rising rate. The type of treatment, whether medical, surgical, or both, depends in part on the height of the rate and whether it is rising or falling. The type of operation, whether ligation of one or more arteries or single or double lobectomy is influenced in the same way —H L

(THYROID) Riedel's sclerotic goiter (Riedelsche eisenharte Struma) Erkes, Klin Wchnschr (Berl), 1922, 1, 1128

In this case, the goiter had shown inflammation. No other details are given —J K

(THYROID) Riedel's sclerotic goiter (Riedelsche eisenharte zione gozzo-cretinica cecitaria) Ferrara (M), Medicina nuova (Roma), 1920, 11, 182-191

During the war Ferrara who was stationed in the Sabbia valley, had opportunity to observe a group of young men manifesting endemic hypothyroid disorders. The family history was determined in one instance. Of the parents and offspring, none was healthy. One daughter was most normal somatically, but an imbecile. Five sons showed varying degrees of goiter, myxedema, dwarfism, mutism or mental retardation, singly or in combination. The author comments on the fact that parents from an endemic goiter region may give birth to normal offspring if they remove to a more salubrious place, whereas previously healthy immigrants to a goiter region may have cretinous offspring, hence some local noxious influence must be postulated —P M N

(THYROID, GONADS) The influence of some endocrine glands on the course of experimental tuberculosis in the guinea pig (Contributo allo studio dell' azione di alcune glandole endocrine sul decorso della tubercolosi sperimentale nella cavia) Ferrata (A), Folia med (Napoli), 1922, 8, 65-67

Ferrata has studied the effects of the transplantation of gonads and thyroid on the course of experimental tuberculosis in the guinea pig. He concludes that subjects lacking the thyroid live a few days longer than the controls, while castration results in still longer survival unless the infection invade the thyroid. In castrated females, tuberculosis manifests itself as in the controls, but in a short time

they recover, increase in weight, and live a long time (ten months in the series reported) —P M N

Anomalies of THYROID function in their bearing upon pregnancy
(Des anomalies de la fonction thyroïdienne dans leurs rapports avec gestation) Fruhinsholz (A) & Parisot (J), Rev franç de gynéc et d'obst (Par), 1921, 16, 603-605

The subject is considered under two chief heads, the experimental and the clinical. The enlargement of the gland seen in pregnant animals is not merely hypertrophy, but also actual structural modification, characterized by rarefaction of the connective tissue and hyperemia. The mechanism of these changes is uncertain, but may possibly be sought in specific substances secreted by the unimplanted ovum and the foetal placenta. Thyroidectomy in early life prevents the development of the genital tract, the uterus and ovaries remaining infantile, in adult life it interferes with fecundation, in the pregnant woman it frequently causes abortion, premature labor, or stillbirth, it may also cause such special complications as tetany. On the other hand, with regard to the effect of gestation, labor or lactation upon the hypothyroid organism, several possibilities are mentioned: (1) no effect, (2) accentuation of the hypothyroidism, (3) tetany, (4) appearance of symptoms in subsequent pregnancies, even though they had not manifested themselves formerly, (5) mitigation of unpleasant symptoms, in certain cases, by injections of thyroid extract. Hyperthyroidism during pregnancy may be mild or it may assume the type of the characteristic Graves-Basedow syndrome. It seems that pregnancy evokes a compensatory hyperthyroidism, especially marked in the second half, and this may become pathologic. Hyperthyroidism is unfavorable to fecundation, but it often shows improvement during pregnancy. Hyperthyroidism may be ameliorated, aggravated or not influenced by gestation —E N

The value of basal metabolic rate determination and the epinephrin test in the diagnosis and treatment of THYROID disorders
Goetsch (E) Long Island M J, 1922, 154, abstr, J Radiol (Omaha), 1922, 3, 298 (See Endocrin, 1922, 6, 59-72)

The writer studied approximately 800 patients suffering from disorders of the thyroid gland. All cases were carefully verified by histological study of operative material, and as a result the writer's clinical test for hyperthyroidism was evolved. In exophthalmic goiter (test usually unnecessary) the epinephrin reaction the writer found to be uniformly positive and parallel with the severity of the symptoms. In colloid goiter without symptoms of hyperthyroidism the reaction is negative. In active adenoma with clinical symptoms of hyperthyroidism the reaction is positive. In obscure cases presenting a hyperthyroid syndrome a positive epinephrin test has often

led the writer to advise operation at which adenomata, too small to be seen or palpated, have often been found and their removal has led to striking benefits. Patients with diffuse adenomatosis are often mistakenly thought to have tuberculosis, neurasthenia, psychoneurosis, effort syndrome, etc., the metabolic rate is not increased in these cases and they are therefore overlooked. A positive reaction to the epinephrin test led to operation in 15 such cases with considerable consequent success. The epinephrin test is also a guide to the amount of thyroid extract administered in cases of hyperthyroidism, myxedema and cretinism. As a guide to differential diagnosis in tuberculosis, psychasthenia, psychoneurosis, hysteria, neurasthenia, dementia precox, melancholia, alcoholism, tabagism, acromegaly and arteriosclerosis as well as in some other disease, the test is of great value as essentially negative results are given. The writer does not hold that the test is absolutely pathognomic of hyperthyroid states—there are a few states which give a more or less typical reaction, but careful history and physical examination clears up such cases. The test is practically always confirmatory, in some other cases diagnostic and in other suggestive. The test is readily understood, performed and interpreted, having an advantage here over the basal metabolic rate test. In mild and latent cases of hyperthyroidism it is more sensitive than the basal metabolic rate test, though this latter is of distinct advantage in early diagnosis of hyperthyroidism and is a very useful guide to the form of therapy demanded by the case in hand, and also functions usefully as a check during treatment. The faulty technique and interpretation of this test are briefly dwelt upon.—R. G. H.

(THYROID) The pathology, diagnosis and surgical treatment of **GOITER** Goetsch (E), Northwest Med (Seattle), 1922, 21, 97-104

Attention is specially directed to the pathologic origin from the alveolar epithelium of colloid goiter, puberty hyperplasia (adolescent goiter) and exophthalmic goiter (Graves' disease), and the nontoxic and toxic adenomata which arise from the fetal or interstitial cells. Large adenomas not infrequently degenerate from a solid into a cystic state and thus spontaneously cure the hyperthyroidism. Goetsch supports the purely surgical treatment of the adenomatous goiter, not having found any improvement from medical, x-ray or radium treatments. He grants a place to these measures where the abnormality consists of alveolar hyperplasia. Diffuse adenomatosis is described as the precise opposite, pathologically, of exophthalmic goiter, the former being a diffuse hyperplasia of the interstitial cells, whereas the latter is a diffuse hyperplasia of the acinar or alveolar cells. Goetsch warns against the expectant treatment of the adolescent goiter girl, strongly advocating surgery both as a curative and prophylactic measure. (Not all thyroid authorities will agree with this attitude.) The value of basal metabolism esti-

mates and the author's epinephrin test in the diagnosis of hyperthyroidism is fully expounded Goetsch being convinced of the absolute reliability of his test believes it preferable to the basal metabolism test, because it is simple, less expensive, and less subject to technical error The author believes in rest, low protein diet and removal of foci of infection, but does not believe that infectious foci ever cause frank hyperthyroidism Their removal improves the general health of the patient which is of course advisable —H L

The incidence of syphilis in HYPOTHYROIDISM and myxedema in children Gordon (M B), N York M J [etc], 1922, 115, 350-252

This study is based upon the examination of the Wassermann and luetin reactions in 42 children suffering from some form of hypothyroidism in an attempt to evaluate the importance of syphilis as an etiological factor in the production of these diseases There were 20 males and 22 females, the ages ranging from 18 months to 10 years Two were positive to both Wassermann and luetin, 2 were positive to luetin, one was positive to Wassermann There were 37 negative tests, making an incidence of 12 per cent A search of the American literature is not conclusive as to the part syphilis plays in the causation of these diseases The results obtained in this series indicate that syphilis is not of great etiological importance in the causation of either childhood myxedema or hypothyroidism in children It is, however, possible for syphilis to attack the thyroid gland with the production of these conditions The presence of a mental deficiency in 3 of the 5 positive cases is significant of the predilection of the spirocheta pallida for the brain and nervous system —Author's Abst

(THYROID) Graves' disease (Morbus Basedow) Gottlieb (K), Wien klin Wchnschr , 1922, 35, 553

A girl of 11 years had an acute goiter, exophthalmos, tachycardia, perspiration, Stellway and Gräfe's symptoms At this age Graves' disease is exceedingly rare —J K

(THYROID) The disappearance of a goiter and improvement of cardiac insufficiency by irradiation of the ovaries (Beseitigung einer Struma und Heilung einer Herzinsuffizienz durch Röntgenbestrahlung der Ovarien Ein Beitrag zur Fernwirkung der Röntgen-strahlen speziell auf endokrine Drüsen) Groedel (F M), Strahlentherapie (Berl u Wien), 1920 10, 1047-1051, abst, J de radiol et d'électrol (Par), 1921 5, 42

The existence of a correlation between the various endocrine glands and of an interdependence of their functions on activity has been discussed many times In particular it has been tried to establish a connection between the function of the ovaries and that

of the thyroid Graf also mentioned the appearance of an exophthalmic goiter following hysterectomy in one case and following destruction of the ovaries by radiotherapy in another. On the other hand, Mannaberg observed excellent results in ten patients suffering from Graves' disease and treated by radiotherapy by Kienbock, and Salzmann has published more recently (1919) an observation on a patient treated by radiotherapy for a fibroid in which a goiter of the size of two fists seemed to diminish very rapidly after existing 15 years, and the tachycardia and diarrhoea to disappear. It seems then that cessation of the ovarian activity might react on the function of the thyroid, more often as a moderator than an incentive, and that this point has not been discussed. Groedel's observation argues along the same lines. A patient examined and treated by him in 1908 for "cardiac insufficiency," with a goiter about the size of two fists, suffered in 1912 with such severe metrorrhagia and anemia that hysterectomy (it was a question of a small fibroid) was judged impossible and radiotherapy advised. Carried out by Groedel with complete success the menopause resulted in three series of sitings repeated after two months (the patient was 45 years old), at the same time that the goiter although large disappeared almost completely and also all the cardiac symptoms. This "action at a distance" of the radiotherapy should be taken into consideration and would justify perhaps an attempt at systematic destruction of the ovaries by radiotherapy in the case of patients suffering from exophthalmic goiter and approaching the climacteric. Analogous attempts seemed equally justified before deciding upon surgical intervention, often dangerous, for the removal of large goiters. They would be the more interesting, seeing that in true goiter direct radiotherapy is generally followed by small enough results.

—Med Sc, 1921, 5, 93

(THYROID) Graves' disease in the mountains (Basedowsche Krankheit in Gebirge) Guhr, Munchen med Wchnschr, 1922, 69, 837

Mountain climate often leads to cure or at least marked improvement in Graves' disease—J K

(THYROID) Goiter in infants (Kropf im Sauglingsalter) Hamburger (F), Munchen med Wchnschr, 1922, 69, 819

Goiter in infants is not rare in Steiermark. It is always a parenchymatous struma. When children with stridor show an increase in the symptom when the head is bent backwards there is probably a substernal goiter. Treatment consists in ointment with iodine and very small doses of NaI by mouth—J K

Differentiation of HYPERTHYROIDISM and of heart disease from neurasthenic states Hamilton (B E) & Lahey (F H), J Am M Ass (Chicago), 1922, 78, 1793-1796

A discussion of differential diagnosis, particularly by careful history taking and physical examination. Basal metabolic rate determination is considered of value in diagnosing hyperthyroidism, while the Goetsch adrenalin test is not.—W M A

A case of **THYROAPLASIA** with reference to certain **ENDOCRINE ORGANS** [Ein Fall von Thyreoaplasia (dystrophischer Thyreohypoplasie) unter Berücksichtigung gewisser der innersekretorischen und lymphoiden Organe. Abteilung I Die innersekretorischen Organe] Hammar (J A) & Hellman (T J), Ztschr f ang Anat [etc] (Berl), 1920, 5, 218-267

Hammar here describes the anatomical condition of parathyroids, thymus, pancreas and suprarenals and ovaries in a child a little over 4 years old with a rudimentary thyroid gland ($2 \times 2.5 \times 2.5$ mm), situated near the foramen coecum. (The second part of this contribution is published by Hellman in Ztschr f Konstit, 1922 8, 336-360.) Histologically the thymus appeared to be in an early stage of accidental involution, the medullary portion, especially, was far below normal in volume, but the absolute volume of Hassall's corpuscles was within normal limits. There being no normal data to compare with his volumetric determinations on the other glands, no conclusions are drawn. The related literature is given.—A T R

A case of **THYROAPLASIA** with reference to certain lymphoid organs [Ein Fall von Thyreoaplasie (dystrophischer Thyreohypoplasie) unter Berücksichtigung gewisser der innersekretorischen und lymphoiden Organe. Abteilung II Die lymphoiden Organe] Hammar (J A) & Hellman (T J), Ztschr f Konstit (Berl), 1922, 8, 336-360

This is the second part of a joint paper (the first part having appeared in Ztschr f ang Anat u Konstit, 1920, 5, 264.) Hellman gives the detailed quantitative results of a determination by a new method of the amount of lymphoid tissue found in the intestines, mesentery and spleen of a 4 yr 3 mo old girl with only a small bit of thyroid tissue measuring $2 \times 2.5 \times 2.5$ mm. In comparison with a single normal case which the author worked up, it appears that the lymphoid tissue in this case of thyroaplasia was below normal, but for want of comparable control data no conclusions are drawn.—A T R

(**THYROID**) Treatment of goiter with faradic current (Faradische Strumabehandlung) Hase (H), Ztschr f phys u diätet Therap (Leipzig), 1921, 25, 29-31

Hase has for several months employed the galvanic current on goiter patients. The quartz rays were also tried. Results were generally unsatisfactory because patients discontinued treatment, owing to the slowness of improvement. Failure of these efforts led

the author to a careful trial of the faradic current. At first, patients with severe Basedow's disease were not accepted, but only those with vascular goiter possessing general Basedowian tendencies. Surprisingly good results were obtained in 8 patients, there was improvement in subjective symptoms and reduction in size of the goiter after six treatments. Thus encouraged, treatment of frankly outspoken cases of Basedow's disease was tried. These also soon began to show favorable changes, the tachycardia, sweating and irritability were improved, but the exophthalmos remained unchanged. There was striking improvement in a case of cystic goiter of several years' duration. A large number of adenomata were apparently influenced to the extent of becoming softer and smaller. Hase thus summarizes his results of the effects of the faradic current. The best results were obtained in vascular goiters, adenomata were more resistant to the faradic current, but showed a tendency to become softer, and in one case there was a disappearance of the pressure symptoms, the faradic current was without results in the retrosternal goiters and in the serious cases of Basedow's disease.—I B

(THYROID) X-ray treatment of Graves' disease (Röntgenbehandlung der Basedowschen Krankheit) Haudek (M) & Kriser (A), Klin Wchnschr (Berl), 1922, 1, 271-276

The authors are quite certain that the x-ray is an excellent method of treatment for Graves' disease. It should be discontinued only when the pulse has become quite stable. The nervous symptoms generally disappear first, then the cardio-vascular symptoms, the diarrhea, the tremor and the perspiration. Often the goiter and the exophthalmos remain unaltered, but there are no other symptoms. Recurrence is not more frequent than after surgical treatment and the mortality is practically nihil. Adhesions are formed only when the x-ray treatment is not carried out in a systematic way. In formes frustes, even in heart neurosis, a good effect may be obtained by x-ray treatment of the thyroid. In Graves' disease it is necessary to expose the thymus also to x-rays. The authors believe that no patient with Graves' disease should be operated upon before an energetic x-ray treatment has been tried.—J K

HYPERTHYREOSEN Hellwig (A), Deutsche med Wchnschr (Berl), 1922, 48, 420-422

Sudeck, in one of his studies on the surgical treatment of Graves' disease, makes the following classification. There is the classical Graves' disease, which is nearly always acute. Then he gives thyroidism, which is chronic and is a real hyperthyroidism. The symptoms in this form closely resemble those after administration of large doses of thyroid. Lastly, status neuropathicus is mentioned. Most of the so-called formes frustes belong to this class. Operation in these cases is never successful. Hellwig criticises this

scheme, however. He does not believe that there is so great a difference between classical Graves' disease and thyroidism. Sudeck (and Chvostek) think that tremor, loss of weight, irregularity of the pulse and eyelid symptoms are typical of thyroidism, but they are also typical of Graves' disease. The blood picture, the adrenalin proofs and the metabolism are the same in both forms. The author examined the histological picture of a large number of goiters and found a marked parallelism between this picture and the intensity of the symptoms. He agrees with the old unitarian view of Mobius that there is no great difference between all the forms of goiter. All are forms of hyperthyroidism. There are light and serious cases. The serious cases are those with symptoms of Graves' disease. According to Hellwig, Sudeck has proved that the serious forms of Graves' disease also also simple hyperthyroidism. This is proved by the fact that Sudeck was able to cure 5 very serious cases by complete removal of the thyroid. (See Janney, *Endocrin*, 6, Nos 5, 6.)

—J K

(THYROID) Surgical treatment of goiter (A propos du traitement chirurgical des goitres). Heismoortel, Scalpel (Brux), 1922, 75, 625-628

Of technical surgical interest. The literature quoted seems to indicate that only in France are goiters operated upon.—J K

(THYROID) The pathogenesis of exophthalmic goitre (Under-søckelser over Mb Basedowii's patogenese). Holst (J), Norsk Mag f Lægevidensk (Kristiania), 1922, 83, 523-538

The author has made serial sections of the thyroid tissue removed by operation, in a number of cases of early exophthalmic goitre and found islands of proliferating thyroid epithelium separated by normal tissue. He therefore concludes that even the diffuse proliferation found in advanced hyperthyroidism of this kind begins like the toxic adenomas as multiple tumor formation. Hence he believes the hyperthyroidism found is primarily due to the histological changes noted.—D J G

(THYROID) Treatment of goiter. Hoag (C L), Calif State J M (San Fran), 1922, 20, 6-8

In treatment of goiter the pendulum has swung from medicine to surgery, and now over toward radiotherapy. The author makes the criticism that much of the treatment is carried on in a perfunctory way, without proper choice of cases and without a knowledge of the general principles essential to intelligent choice of therapeutic measures. Too many who have little experience even in general therapy are giving treatment for this malady. Diagnosis of thyroid disease is only the first step—it is just as necessary to recognize clearly the various forms of thyroid enlargement as to distinguish between different forms of intestinal parasites. For practical

purposes the following classification meets all requirements (1) atoxic, (a) simple hypertrophy, adolescent goiter, (b) colloid, calcified or cystic, (c) simple adenoma, (2) toxic, (a) toxic adenoma, (b) hyperplastic (exophthalmic), (3) malignant, (a) carcinoma, (b) sarcoma, etc. In well developed cases it is easy to determine the classification of the goiter, but many border line cases give only mild symptoms and a large goiter may be deficient in thyroid secretion while a barely perceptible gland often is producing an extensive degree of hyperthyroidism. Since the thyroid secretion seems to be the principal regulator of the metabolic processes of the body an accurate estimate of its activity is secured by determining the basal metabolism in goiter patients. Many diseases influence the metabolic rate, but the influence of goiter is most striking. In the Crile and Mayo clinics radical operation is not done in toxic cases until the basal metabolism is less than plus 50%. Medical treatment, ligation of the superior thyroid arteries and x-ray are used until this point is reached, and even then the time of the operation must be determined by the phase for each indicated. The author believes x-ray or radium therapy is indicated in simple hyperplasia and hyperplastic goiters only, and contra-indicated in colloid, cystic, nodular and adenomatous types. Treatment of goiter is essentially surgical, medical treatment. Roentgenotherapy and radiotherapy are sometimes curative and are often helpful in decreasing thyroid activity and in preparing the patient for operation —J Radiol, 3, 117

(THYROID) Technic of operation for goiter to improve postoperative cosmetics. Hunt (J), Northwest Med (Seattle), 1922, 21, 104-107

Before the patient enters the hospital, the head is flexed half way to the chest, and with a 15 per cent silver nitrate solution on the butt of a straight needle, dots are placed at intervals along the natural crease of the neck. Incision is made later along the line of these black dots. The reader is advised to consult the article for further details of technique in operating, and closure of the wound—all contributing to immediate union, symmetry of the neck and almost invisible scar. The article is illustrated with several photographs —H L

The THYROID General surgery Hubeny (M J), Pract Med Series, 1921, 226

X-ray treatment of exophthalmic goiter is not to supercede surgery, but rather it is preferred in certain types because the percentage of cures is as great as following surgery. The earlier the cases are treated, the better the results. Favorable signs are lessening in nervous symptoms, lowering of the pulse rate, and disappearance or improvement in exophthalmos. The goiter might or might not decrease in size. In ambulatory cases there is no inter-

ference with the daily occupation In marked thyrotoxic cases it is essential to regulate diet, to provide for mental and physical rest Focal infections should be removed and special attention paid to the teeth Some of the undesirable and dangerous possibilities were hypothyroidism, telangiectasis, and atrophy of the regions treated Telangiectasis is more liable to occur in young women, and also if the filtration is insufficient or if erythema is produced several times In discussing this paper, A J Ochsner stated that fifteen years ago this treatment was suggested Many cases improved but none of them seemed to show permanent improvement Now the case is different The technique has been worked out, the physics is understood, and by giving attention to the thymus gland something definite can be done —Abst, J Radiol 3, 113

HYPOTHYROIDISM and the vicious circle Hurry (J B), Practitioner (Lond), 1922, 103, 283-294

Cretinism, endemic goitre, myxedema and minor thyroid insufficiency are described with their resulting derangements of growth and function in almost all the systems of the body The author then suggests that these very alterations and abnormalities in turn repercuss as it were on the diseased thyroid, further depressing its activity, thus producing a vicious circle —H L

(THYROID) Report of radium cases of head and neck Jones (A C), Northwest Med (Seattle), 1922, 21, 140-143

The author treated four cases of goitre with radium A brief note is given of one woman aged 37, pulse 160 basal metabolism 146 plus, who was treated with 50 mg of radium for two hours, screened with 1 inch of wood and 1 mm of lead, over one area The same screening with 75 mg for three hours over two large areas was used In three weeks basal metabolism had dropped to 41 plus The same treatment was repeated Two weeks later the pulse was 85 and basal metabolism plus 6 The remainder of the article deals with conditions treated by radium, such as cataract cancer of lip, etc, and is not of endocrine interest —H L

The control of x-ray therapy in HYPERTHYROIDISM by the basal metabolism test Jones (H M), J Radiol (Omaha), 1922, 3, 85-92

The metabolism of the human organism may be defined as the sum total of the chemical changes going on in the cells of the body To measure the rate of metabolism it is necessary to measure either the rate of heat production or the rate of chemical interchange above mentioned This reduces to the task of measuring the oxygen intake The final result is stated in terms of a plus or minus per cent of the patient's so-called normal rate Muscular effort and food absorption have an effect upon the rate, therefore the test is preferably given

in the morning before breakfast, and with the patient lying down for from twenty to thirty minutes before the test is made. A concise table giving rates of metabolism for both sexes and for ages from six years to eighty has been compiled by Aub and DuBois. Any deviation of ten per cent from the normal rate is the basis of diagnosis for some twelve to fifteen pathological conditions of which there may be combinations. The test is used only for diagnosis of thyroid and pituitary abnormalities because the diagnosis for other conditions in which it might apply is more easily made by other means. It must be kept in mind that in a suspected case of hyperthyroidism these other pathological conditions may be affecting the metabolic rate, and also that in the presence of symptoms suggesting some other pathological condition the basal metabolism test is the only means of recognizing the beginning of hyperthyroidism. Froelich's syndrome can often be distinguished only by means of the test. Addison's disease is often confused with myxedema and thyroid therapy controlled by metabolism determination will differentiate these. The test is most valuable in border line cases. As to its being an index to operation the Mayo brothers believe that a patient showing a metabolic rate of plus forty per cent with an upward rate is a more dangerous risk than one with a rate of plus sixty and a downward rate. Age, nutrition, condition of the heart and other factors must also be taken into consideration. The surgeons' objections are that much of the gland may be destroyed, thus causing hypothyroidism, also many patients show no response to the treatment and the delay is made at the expense of myocardium. The radiologist in reply objects to surgery on the same grounds. Personal opinion and wrong diagnosis at the outset is responsible for many false conclusions. Also irregularity of dosage and variations in technique have led to a multiplicity of opinion for and against roentgen ray in hyperthyroidism. The secretion of the thyroid is unquestionably diminished by x-ray treatment, and, following wrong diagnosis, havoc has sometimes been wrought. Too small or too large dosage likewise brings disaster. A more perfect dosage is yet to be developed. The advantages are summarized as follows: No fatalities, no scar, no interference with the patient's occupation, it is painless, and if it is unsuccessful an operation will be less difficult. Means and Aub believe that surgery should be employed only after roentgen rays and other methods have failed. Some one hundred or more investigators show that the roentgen rays have a curative effect on hyperthyroidism. The most important uses of roentgen ray in these cases are in treatment of those showing a minor degree of toxicity and reducing the toxicity in more severe cases previous to operation—Abst., J. Radiol., 3, 111.

(THYROID) Experimental transformation of an axolotl into an amblyostoma. Kolzov (N. K.), Bull. Inst. Exper. Biol. (Moscow), 1921, 1, 68-72.

This was accomplished by feeding on thyroïdin. Many details are given and much theorizing—e. g. he attributes the general emaciation of the population of Russia since 1917 in a great part to hyperthyroidism, provoked by nervous shocks.

—Physiol Abst 1922, 7, 195

The action of **THYROIDECTOMY** and castration upon the islets of Langerhans. Konevskaja (E. O.), Med Sc (Lond) 1919, 3, 286-291

Five dogs showed, after thyroidectomy and castration, an increase in number and an enlargement of the islets as compared with normal dogs—Physiol Abst, 1922 7, 194

(**THYROID**) Importance of basal metabolism determinations and the test of induced hyperglycemia in the diagnosis of Basedow's disease (Importance de la mesure du métabolisme basal et de l'épreuve d'hyperglycémie provoquée pour le diagnostic de la maladie de Basedow) Labbé (M.), Stévenin (H.) & Nepveux (F.), Bull et mém Soc méd des hôp de Par 1922, 46, 902-911

A review of personal observations confirming the results of the American workers—F. S. H.

A review of a year's **THYROID** work. Lahey (F. H.), Boston M & S J, 1922, 186, 562, abst, J Radiol (Omaha), 1922, 3, 297-298

The writer believes that many errors in thyroid treatment are made because of inadequate knowledge of the clinical classification of thyroid disease and ignorance of the indications for operation. So-called adolescent goiter with slight enlargement requires no treatment. Colloid adolescent goiter seen in goiter belts is a different type. There is necessarily a relation between tachycardia and enlargement when both are present. Tachycardia of thyroid origin does not exist without other signs of this disease. The two conditions may exist even with a moderate increase in the basal metabolic rate without hyperthyroidism being present. If hyperthyroidism is present tachycardia and increased basal metabolic rate will be present also, but goiter may exist without hyperthyroidism, and vice versa. Colloid goiters and cysts, when unsightly or intra-thoracic or associated with hyperthyroidism, Lahey would operate upon, also upon the latter when they produce pressure. Adenomata he believes should be operated upon if they are producing secondary hyperthyroidism or if they present danger of malignancy, this latter being especially stressed. Hyperthyroidism has not occurred in this group (five hundred cases) without an increase in basal metabolism rate, operations undertaken upon patients with normal metabolisms will yield consistently poor results. It is a grave error to consider thyroid disease in terms of increased metabolism, and metabolism test can be of as much harm as good unless carefully weighed and

correlated with the history and clinical signs presented by the individual. Most hearts in hyperthyroidism show no signs, upon clinical examination, of heart damage, but a smaller class shows definite signs of this. The writer's attitude toward x-ray therapy is exceedingly skeptical. Experimental work tried out under his management and with his selection of cases and interpretation as to cure or relief at the Boston City Hospital, leads him to conclude that surgery is preferable. He states, however, that the cases have been limited in number, and that as a clinician and not a trained roentgenologist, he has had no check upon the dosage, but he immediately counters this statement by one asserting absolute confidence in the accuracy of the dosage employed by the roentgenologist in charge.

—R G H

Multiple stage measures in the surgery of severe HYPERTHYROIDISM Lahey (F H), J Am M Ass (Chicago), 1922, 78, 1862-1865

By the use of such methods the author reports a mortality of 1.17 per cent in 342 thyroid operations —W M A

Three cases of HYPOTHYROIDISM Law (W F), Tr Roy Acad Med Ireland (Dubl), abst, Irish J M Sc (Dubl), 1922, 5 s, 142

The first case was that of a woman, aged 60. The most striking features were hemorrhage from the bowel, and scantiness of the eyebrows in the outer third. The patient was also getting stouter and had a subnormal temperature. In the second case (a woman of 30) the patient complained of an almost constant feeling of chilliness with attacks of migraine. The attacks of migraine stopped during pregnancy and lactation, and then recurred. In the third case (a man, aged 29) there were slight neuralgic pains, scantiness of the outer third of the eyebrows, loss of energy and increase in weight. All three cases recovered completely on treatment with thyroid extract —Quoted

THYROID medication and hypotrophic infants (Médication thyroïdienne et nourissons hypotrophiques) Lesné, Bull gén de therap [etc] (Par), 1922, 173, 271-272

Lesné uses pluriglandular as well as thyroid therapy in disturbances of growth in infants. He gives daily for 10 days 0.02 gm each of thyroid, hypophysis and adrenal powder and repeats after an interval of 10 days —F S H

Methods of estimating the activity and intelligence of normal and THYROIDECTOMIZED sheep Liddell (H S), Proc Soc Exper Biol & Med (N Y), 1922, 19, 343-344

Of technical interest —R G H

The effect of **THYROID** feeding on the bone marrow of rabbits Llm
(R K S), Sarkar (B B) & Brown (Jane P H G), J Path &
Bactriol (Cambridge), 1922, 25, 228-246

This investigation "is an attempt at a detailed cytological examination of the bone marrow, in an endeavor to determine the part played by it in the causation of the variable changes in the circulating blood corpuscles after thyroid feeding" Twenty rabbits were given daily doses of the desiccated thyroid powder of the British Pharmacopoeia The conditions of the experiments were the same for all animals, as to time of feeding, time of taking blood counts, etc For enumerating the marrow cells, marrow from the shaft and epiphyses of the femur was fixed in various fluids imbedded in paraffin, and cut in sections 5 microns thick The most useful stains were found to be "the Romanowsky combinations, especially alcoholic eosin and methylene blue, and Giemsa" A number of squares, each 2 by 2 mm were ruled on a cover glass and this was inserted in the eye piece of the microscope By adjusting the tube length, using the oil immersion lens and a stage micrometer, the microscope was set so that each square represented an area of 0.0025 sq mm A minimum of 500 cells was counted, and from this the percentage of each type of marrow cell was determined The bone marrow of young rabbits was found to differ from that of adults in containing fewer cells, and in exhibiting a higher percentage of polymorphonuclears than of small mononuclears Thyroid feeding invariably caused an increase in the percentage of polymorphonuclears and a diminution of the small mononuclears, which is most marked in young individuals In older animals and on continuing the treatment, the percentage of polymorphonuclears in the marrow falls and may become subnormal, while the percentage of mononuclears recovers and may be above normal Daily doses of 0.25 to 0.5 gram per kilo of thyroid increase the total number of marrow cells, but larger doses may not do so, the qualitative changes, however, are always similar Blood counts, red slightly and white more distinctly, are raised in young rabbits only, no changes occur in older animals except after prolonged feeding when a slight fall may occur The differential count shows a marked relative polymorphonuclear increase in the young, and transitory and less marked increase in adult rabbits The mononuclear percentage shows a fall when the polymorphonuclear percentage rises, but it does not show any rise above the normal even after prolonged feeding These changes are not so constant in animals given heavy doses (i e, more than 0.6 gm per kilo), of thyroid As to the significance of these findings, it is suggested (a) that the bone marrow is stimulated to activity under the conditions of these experiments, resulting in the increased production of polymorphonuclears and small mononuclears, according to the age of the animal The mononuclears, however, do not reach the circulation as

such, since there is never any obvious increase in the number of blood mononuclears after prolonged thyroid feeding. They must therefore undergo development into another type, namely, erythroblasts and eventually erythrocytes. (b) That increased production in the marrow should lead to an increase of the corpuscles in the circulation. This is not evident from the blood counts, but may be masked by some such factors as an increased destruction of cells, an increased blood volume, circulatory changes, etc. (c) That the marrow mononuclears are not responsible for the supply of mononuclears to the blood stream and therefore do not function as lymphocytes.—J P S

(THYROID) Fats in relation to the genesis of goiter. McCarrison (R), Brit M J (Lond), 1922, i, 178-181

This author first summarizes a previously reported (Indian J M Research, Jan 1920) experimental study of the thyroid weights in groups of pigeons fed with fat in form of butter, where he found goiter present in 65% of the birds fed with butter fat, and that the histology of these thyroids resembled that found in the thyroids from cases of Graves' disease. The present paper deals with a similar study in which pigeons and tadpoles were used. The hygienic surroundings were not as perfect as in the previous experiments and the work was done in a region (Oxford, Eng.) known to be in a goiter belt. Twenty-eight birds were used and the feedings consisted of 50 gms of mixed grains, to which was added 16 cc of oleic acid for 7 birds, 4 gms of butter fat to the food of 7 others, and 1 dram of cod-liver oil (containing 0.002% iodine) to the ration of 7 others, while the remaining birds were fed on the mixed grains. At the end of 143-144 days the pigeons were killed and the average weights of the thyroid glands noted. The glands from the controls averaged 537 mgs, those fed with butter fat 675 mgs, those with oleic acid 909 mgs, those with cod-liver oil 93 mgs. McCarrison calls attention to the marked difference in the weight of the thyroids from pigeons fed on cod-liver oil. To determine the relation of fat excess and iodine intake, groups (50) of tadpoles were fed with a flour caseinogen mixture to which was added butter fat, oleic acid, cod-liver oil, or varying amounts of iodine. An excess of fats caused remarkable retardation in the growth of the tadpoles. The iodine in amounts of 0.5 to 1 gm per gram of food tended to prevent the retardation of growth induced by the butter fat and oleic acid, but not that caused by the cod-liver oil. The retardation of growth induced by the fats was associated with a delayed development of the thyroid gland. McCarrison states that he believes that the composition of food has an important bearing on the genesis of goiter, that food must be considered both in its relation to its content of available iodine and in its relation to its content of fats, that variations in the histologic types of goiter may result from the variations in the composition of goiter inducing foods.—F C P

(THYROID) The rôle played by the physician and surgeon in the treatment of Graves' disease McKay (W J S), Med J Australia (Sydney), 1920, II, 357-359

A general discussion of therapeutic procedures—R G H

(THYROID) Roentgen ray treatment of toxic goiter Means (J H) & Holmes (G W), Tr Ass Am Physicians, May 2-4, 1922,

Of 44 cases of exophthalmic goiter, definite improvement was secured by roentgenotherapy in 28. Sixteen showed little or no improvement, eight of these patients later came to operation and were apparently cured. Of the 28 in which there was improvement, there were 13 who were apparently cured, and 15 who were improved but not rendered entirely free from hyperthyroidism. No patients seemed to be made worse by the treatment. Two patients improved but not cured were operated on later. One of these died after operation. Of the 12 toxic adenoma cases treated by roentgen rays, all showed improvement and 5 patients were apparently cured. Two of the exophthalmic and one of the toxic adenoma cases developed myxedema during roentgen ray treatment, which was promptly relieved by thyroid administration, and in the two exophthalmic patients the depression was only temporary, as thyroid was later discontinued without a return of myxedema. In those cases of exophthalmic goiter which respond to roentgen rays there is a rapid fall in pulse (average from 115 to 89) and in basal metabolism (average from + 55 to + 21 per cent), and a corresponding gain in weight (average of 9 per cent) in the first 4 months of treatment, during which time they receive on an average 5 treatments. In some cases the curves come to a normal level, in others they do not. In the latter further roentgen ray treatment is not strikingly satisfactory except in the cases which show a definite relapse, in these a second course of treatment may act as did the first. We have as yet found no method of predicting which cases will respond to roentgen rays. The results in toxic adenoma are similar to those in exophthalmic goiter. In general, we feel that roentgen rays may cure certain cases, that it may improve others, that for this reason it has its place in the treatment of toxic goiter. If it does not secure good results in a few months, surgery should be employed. Some patients who are not cured by roentgen rays are rendered better operative risks. A combination of roentgen rays and surgery will sometimes accomplish more good than either form of treatment alone. To make a proper use of the roentgen rays in the management of toxic goiter, its limitations must be recognized and, when necessary, it should be combined intelligently with surgical procedures.

—J Am M Ass, 1922, 79, 67

Cancer & opothérapie Naamé, Gaz d hôp (Par), 1921, 94, 170-172

Two cases diagnosed as epithelioma showed recovery after taking bile, thyroid and pancreatic extract in combination. The author repudiates a suggestion that the neoplasms were syphilides that healed as a result of iodine (thyroid) medication—R G H

Effect of THYROID colloid on tubercle bacilli Nathan (K), *Ztschr f Tuberk (Leipz)*, 1921, 34, 390-391

The rarity of thyroid gland tuberculosis may be due to an inhibitory action of its secretions, especially of the colloid of the gland. With this in mind the colloid was pressed out of thyroid gland substance and graded quantities of tubercle bacilli were mixed with it and exposed for from 4 to 24 hrs at 37° and then injected into guinea pigs. The injected animals, however, showed no longer duration of life than the control animals—Chem Abst, 16, 1617

(THYROID) A case of goiter recurrence (Rezidiv von Basedow) Neupert, *Klin Wchnschr (Berl)*, 1922, 1, 1232

Some time after hemistruumectomy the other half of the thyroid became enlarged. The arteries were so strongly developed that the rest of the thyroid looked like an angioma arteriale racemosum—J K

(THYROID) Basedow syndrome and trophic edema (Syndrome de Basedow et trophocdeme) Parhon (C J) & Stocker (A), *Rev neurol (Par)*, 1920, 27, 1020-1031

A female, single, aged 21, had had an onset of illness 2 years before, following a fright. There was a gradual development of Basedow's disease with palpitation, tachycardia, tremor, swelling of the thyroid, exophthalmos, headaches, irritability, nausea, vomiting, insomnia, dyspnoea, and weakness. Treatment was variegated, including bromides, iodides, arsenic, thyroid extract, antithyroidin, and 8 months' rest in bed, with but slight improvement in the general condition during the administration of arsenic. Edema beginning at the instep was observed. This soon extended upward, involving the entire lower limbs, and was attributed by the patient to the obesity which developed during the arsenical treatment. The infiltration of the lower limbs inhibited their power of locomotion and the usual actions of the day, such as getting off and on the bed, sitting down, etc., became extremely difficult, resembling the movements of a case of myopathy. There was no change in color or temperature of the skin and no pitting on pressure. The diagnosis of trophic edema complicating Basedow's disease was made. Such an association is rare, the author in perusing the literature could find but 25 such instances recorded. The article contains a valuable review of the subject of trophic edema and allied conditions, with causal theories advanced by the numerous authors mentioned in the bibliography—I B

Organic reactions and **THYROID** extracts in disturbances of the thyroid function, "the thyroid sign" (Réactions organiques et extraits thyroïdiens dans les troubles de la fonction thyroïdienne, "le signe de la thyroïde") Parisot (J) & Richard (G), Bull et mém Soc méd des hôp de Par, 1922, 46, 806-810

The authors studied the effects of thyroid extract injections on 72 persons distributed as follows 17 Basedowians and patients with hyperthyroidism, 32 persons of normal gland function, and 12 persons presenting signs of hypothyroidism The general observation is that a massive injection of 1 gm of thyroid extract may produce modifications in the pulse, arterial tension and oculo-cardiac reflex The pulse of the normal individuals is not changed beyond normal limits of variation by thyroid administration Hyperthyroid cases respond by a slowing of from 10 to 30 beats, while hypothyroid cases of all types do not respond or if at all, by a slight acceleration The oculo-cardiac reflex is not significantly altered in normal persons subjected to injection of thyroid extract, while persons exhibiting hyperthyroidism show a slowed positive reaction and in those with hypothyroidism the reaction is reversed In normal persons and those with hypothyroidism the injection of thyroid extract does not modify the maximum arterial tension, but raises the minimum for 10 or 15 minutes In hyperthyroid cases, however, the minimum is not affected, but the maximum drops from 20 to 40 mm These reactions were obtained from deproteinized extracts and are interpreted as vagal in origin The "thyroid sign" is the response by hyperthyroid patients to the injection of thyroid extract

—F S H

(**THYROID**) Treatment of goiter (Traitement des goitres) Pauchet (V), J de méd de Par, 1921, 40, 81-84

This is a review of the applied anatomy of the thyroid with respect to goiter, and of the operative technique advised by the author The article is of no general endocrine interest, but may be found of service to the surgical technician —I B

(**THYROID**) Differential diagnosis of diseases of the mediastinum Phillips (J), J Am M Ass (Chicago), 1922, 78, 1355-1363

Intrathoracic thyroid is considered among other tumors of the mediastinum for differential diagnosis and one case is reported in detail —W M A

(**THYROID**) Must the wound after strumectomy be closed or drained (Volliger Wundschluss oder Wundschluss mit Drainage nach Kropfoperationen)? Propping (K), Zentralbl f Chir (Leipz), 1922, 49, 829-830

Of technical, surgical interest —J K

(THYROID) Goiter prophylaxis in Bern (Kropfprophylaxe in der Stadt Bern) de Quervain & Lauener, Klin Wchnschr (Berl), 1922, 1, 344

In Bern 73.2% of the children of 7 years have an enlarged thyroid, 34.7% have even a very large thyroid. Of the children of 15 years 93-94% have a palpable gland. Thus the so-called "school prophylaxis" is no prophylaxis but a real treatment. There are several different forms of prophylaxis in the schools in Switzerland, all of which bring good results. Iodine is put in open vessels in the school rooms or it is given as amulet to the children. Very small doses of iodine salts or of iodine containing fatty acids are given. It is theoretically not impossible that the number of cases of Graves' disease may slightly increase, since serious Graves' disease is especially seen in countries without endemic goiter.—J K

(THYROID) La coexistence de l'endémie goitreuse et du syndrome de Basedow dans un village des Hautes-Prénées. Regnault (F), Soc de méd de Par, April 14, 1922, abst, Presse méd (Par), 1922, 30, 361

Graves' disease in this village is often complicated by goiters brought about by pregnancy or excitement or by no appreciable cause at all.—R G H

(THYROID) Quantitative studies on the action of thyroxin, diiod-tyrosin, jodothyryn and jodthyreo-globulin (Quantitative Untersuchungen über die Wirkung von Thyroxin, Diiodtyrosin, Jodothyryn und Jodthyreo-globulin). Romeis (B), Klin Wchnschr (Berl), 1922, 1, 1262

The author studied the influence of these substances on the development of tadpoles. Thyroxin proved to be very powerful in producing a quickened development. Its action is the same in young or old tadpoles. Much more diiodtyrosin, however, is required to accelerate development in old than in young tadpoles.

—J K

(THYROID) Basal metabolism of patients with Graves' disease after x-ray treatment (Respirations—Stoffwechselversuche an Röntgen-behandelten Basedow Kranken). Roth (N), Wien Arch f innere Med, 1922, 8, 367-378

The author reports 4 cases of classical Graves' disease and one case of formes frustes (exophthalmos, tremor, restlessness, Kocher's blood picture, but with normal metabolism and without alimentary glucosuria). In three cases of Graves' disease, especially in an acute case, the highly increased basal metabolism became normal and the complaints of the patients disappeared. In a fourth case x-ray treatment had no effect. In the formes frustes metabolism was normal and remained unaltered by treatment,

though the patient became more quiet after treatment, the other objective symptoms did not improve —J K

(THYROID) Hyperthyroidism with use of Goetsch test and glucose tolerance determination in diagnosis Rucks (W W), J Oklahoma M Ass (Guthrie), 1921, 11, 93

Rucks reports a case in a married female of 27, in which the main features were nervousness, loss of weight, hyperidrosis, tachycardia, palpitation, dyspnoea, and disturbed sleep. The apparent duration of the illness was 18 months. Teeth and tonsils presented evidences of focal infection, the thyroid was enlarged, the heart sounds were snappy in nature, there was a tremor of the outstretched fingers and hyperactive reflexes. The patient's history revealed the fact that she had been given ten grains of sodium bromide daily by another physician for a long time. A diagnosis of hyperthyroidism was made, although some of the symptoms were attributed to the prolonged use of bromides. Treatment consisted in tonic and dietetic management, with the administration of sodium chlorid as an antidote for chronic bromide poisoning. After a preliminary stay in the hospital the patient was sent home. Within 3 months she returned to the institution, when both the Goetsch adrenalin test and the glucose tolerance test proved positive. A subtotal resection of thyroid was advised —I B

(THYROID) Prognosis in mental disease Rutherford (H R C), Tr Roy Acad Med Ireland, Sect Med, abst Irish J M Sc (Dublin), 1922, 56, 93-94

For purposes of comparison, the author made a classification of states, instead of entities. He divided them into four types—depression, excitement, confusion and delusion. An analysis had been made of 157 recoveries. A depression state was present in 63 cases. The general recovery rate, as estimated upon the admissions, had worked out at 43.13%. Permanence of recovery was not to be found, as a rule, in mental disease, owing to the influence of heredity. Heredity was usually to be discerned in from 50% to 70% of admissions. This heredity he regarded as being purely of a hypothyroidal nature. He had come to this belief by the large number of patients, with an early psychopathic inheritance, who responded to thyroid treatment. Especially was this to be noticed in cases showing a family history of collateral heredity. The later hypothyroidal generations showed dementia praecox and imbecility, which conditions were accompanied by degenerative changes, or undevelopment, and these the late administration of thyroid could not remove. He commented upon the influence of thyroid in the organism's growth, and suggested that the want of durability in degenerated tissues was due to deficient thyroid, so that when strain came the affected organ failed. Hypothyroidism only acted as a predisposing cause, but whenever the exciting cause of the mental

attack was a feeble one, the administration of thyroid would remove it. There was a marked association in both the insane and their relatives, of tuberculosis, asthma, and malignant disease. The author suggested that defective thyroïdal secretions might act as an hereditary and predisposing cause in these diseases also. Infections of all sorts, especially intestinal, are very common in the insane, and he thought, due largely to the hypothyroid state. The thyroid, and occasionally, the suprarenal, were the only glands which had given him results —Quoted

The rôle of the **THYROID** gland in otolaryngology. Schatz (H. A.), Penn. M. J. (Harrisburg), 1922, 25, 529-538

The subject is considered under the following headings: hemorrhage, epistaxis, affections of the nose and asthma, the mouth and fauces, the tonsils and adenoids, headache and migraine, the voice and larynx, the ear and deaf-mutism, diagnosis, pathology, treatment, drugs, clinical studies. Twenty-four articles are collected in the bibliography and repeated references to them are made throughout the article. As the article itself is largely an abstract, it hardly lends itself to further condensation. An interesting discussion of this paper and those of Fridenberg and Zentmayer follows —H. L.

The influence of the **THYROID** on metabolism with especial regard to heat regulation (*Über den Einfluss der Schilddrüse auf den Stoffwechsel mit besonderer Berücksichtigung des Wärmehaushalts*). Schenk (P.), Arch. f. exper. Path. u. Pharmakol. (Berl.), 1922, 92, 1-21

The metabolism of a thyroidectomised rabbit differs greatly in starvation from that of a normal rabbit. While in the thyroidectomised animal the CO_2 output diminishes greatly, the oxygen intake diminishes much less, so that the author records a respiratory quotient at times less than 0.5. The urinary nitrogen is much less in the starving thyroidectomised animal, and consequently it lives much longer than does the starving normal. The intravenous injection of thyreoglandol (used as the active principle of the thyroid gland, though stated to be almost iodine-free) is claimed to produce a large rise of metabolism in the thyroidectomised animal, but not in the normal animal (a claim hardly borne out by the figures given). The influence of thyroid in heat regulation is demonstrated by the fact that a starving thyroidectomised animal cooled to 33° took 1 hour longer to return to normal than did a starving normal animal cooled to 36°. Finally, the serum of a cooled animal, rich, according to the author, in thyroid hormone, was without effect on a second normal animal until this second animal was thyroidectomised. The serum of the cooled animal injected into the second

then produced a large rise in metabolism. Serum taken from a cooled thyroidectomised animal was ineffective.

—Physiol Abst, 7, 256

A case of congenital **ATHYREOSIS** (myxedema) with special regard to muscular alterations (Ueber einen Fall von Athyreosis congenita (Myxodem) und besonderer Berücksichtigung der dabei beobachteten Muskelveränderungen) Schultz (A), Virchow's Arch f path Anat (etc) (Berl), 1921, 232, 302-315

A report of a case of congenital myxedema in a female child of 7 years. Thyroid medication, begun less than a month before death, which was due to broncho-pneumonia, resulted in "greater liveliness" and increased interest in her surroundings. At necropsy no trace of thyroid tissue could be found although there was a small cyst filled with clear fluid in the region of the right lobe of the thyroid. Three parathyroids were present and apparently normal on microscopic examination. The thymus was small, the differentiation between cortex and medulla indistinguishable, and Hassall's corpuscles were few in number and small. The hypophysis, adrenals and pineal gland showed nothing noteworthy. There were numerous large islands of Langerhans in the pancreas. The ovaries showed many well developed follicles. In the muscle of the tongue and of the thigh, Schultz found great variations in the width and a varicose distortion of the fibers. In some fibers there was herniation of the sarcoplasm. The striations were lost. In places there was a proliferation of the sarcolemma nuclei, in other places the nuclei were shrunken and pyknotic.—J P S

(**THYROID**) Keratitis diffusa fetalis (ichthyosis congenita) Hess (J H) & Schultz (O T), Am J Dis Child (Chicago), 1921, 21, 357-389

Hess and Schultz report a case in a child one day old who died eight days later. Because of alterations which occur in the skin in conditions of loss of thyroid function, it would seem pertinent to consider the possibility of relationship of abnormality of thyroid function to keratitis diffusa fetalis. Absence of or failure of development of the thyroid has been noted by Winfield and by Moore and Warfield. In Wassmuth's case, the parents were high-grade cretins. In Moore and Warfield's case the thymus was atrophic and fibrous. In Hess and Schultz's case the thymus showed no striking deviation from normal, except richness in Hassall's corpuscles, but the thyroid gave definite morphological evidence of loss or absence of function. With the exception of four small and relatively insignificant areas, the thyroid was totally undifferentiated. It was composed of small cells without any follicular arrangement and with no formation of secretory material except in the small areas noted. In general, the abnormality of the thyroid in this case appeared to

be of the same nature as in the case noted by Moore and Warfield. The condition of the thyroid is striking and suggestive, but thyroid deficiency cannot be considered an essential factor in keratitis diffusa fetalis unless it occurs more frequently or more uniformly than the previous literature indicates. None of the other glands of internal secretion showed any deviation from the normal which might be held to have any relation to the general condition.

—M B G

(THYROID) Treatment of Graves' disease (Behandlung der Basedowschen Krankheit) Schloessmann, Klin Wchnschr (Berl), 1922, 1, 243

See Endocrin, 1922, 6, 472 —J K

(THYROID) Certain actions at a distance produced by x-rays (Di talune azioni a distanza prodotte dei raggi X) Serena (M), Radiol med (Torino), 1920, 7, 203

A study of the effects of small or medium doses of x-rays which produced distant changes when applied to certain glands, apparently through the medium of an action on the internal secretions. Cases are quoted to show how a series of small stimulative doses applied to the thyroid or genital glands led to correction of menstrual functions and the clearing up of psoriasis and other dermatoses. The author regrets that there is no clue as yet to the proper dose of rays to the thyroid for procuring restoration of normal menstruation —Med Sc, 1921, 3, 476

Activity of the THYROID gland and immunity processes (Sulla attività della ghiandola tiroide nel processo immunitario) Sestini (C), Sperimentale Arch di biol (Firenze), 1922, 76, 79-86

Sestini studied the histological and histochemical modifications of the thyroids in guinea pigs vaccinated with the Eberth bacilli. He observed hyperemia of the gland, increase of the colloidal substance and of the epithelial cell volume, turgid nuclei, cells rich in fuchsinophil granules and, especially, augmented lipid granules —in short, evidence of hyperfunction —P M N

THYROID The surgical treatment of exophthalmic goitre Shawan (H K), Grace Hosp Bull (Detroit), 1921, 5, 8-14

With Plummer's classification as a basis, Shawan discusses hyperplastic and adenomatous goitre, stating that in mild or moderate stages, removal of all sources of infection and medical treatment should be tried, but advocating radical operative treatment in severe, or serious stages, as well as in cases of moderate toxicity not improved by rest. Crile's operative technique is followed. The author stresses the fact that adenomata are always surgical, and that clinical judgment must supplement laboratory tests of toxicity

—C R

(THYROID) Goiter operation technique Sloan (E P), Illinois M J, 1921, 30, 130-133

The writer regards associated heart pathology as the only definite bar to removal of a diseased thyroid, and where auricular flutter or fibrillation are present, prefers gland injection, or ligation of the inferior thyroid arteries to ligation of the superior thyroids. The technique of local anesthesia thyroidectomy, which he now uses in all cases, is given in detail. Removal of the entire diseased portion, the whole gland if necessary, is urged, and surgery is advocated in all cases as reliable, prompt, and, under local anesthesia, comparatively safe —C R

(THYROID) Case of exophthalmic goiter Smith (E B), Proc Roy Soc Med (Lond), 1922, 15, 30

This is the report of a girl, aged 13½ years, who was taken to a throat hospital on account of some difficulty in swallowing. In the course of time a definite diagnosis of exophthalmic goiter was made. The case is reported because of the infrequency with which the disease occurs in children —I B

(THYROID) Technik der Strumektomie Streissler, Klin Wehnschr (Berl), 1922, 1, 1128

A few technical details are given —J K

X-ray treatment of the THYROID (Bestrahlungen der Thyreoiden) Szego, Deutsche med Wehnschr (Berl), 1922, 48, 888

There is no marked reaction after injection of adrenalin after the thyroid has been exposed once or twice to x-rays —J K

(THYROID) X-ray treatment of Basedow's disease Trostler (I S), Am Physician (Rahway, N J), 1921, 26, 289-291

The author, a roentgenologist, is opposed to the medical treatment of Basedow's disease on the grounds that only 20% of the patients are cured, and in these relapse is common. He is opposed to surgery because the operative risk is too great. He claims that x-ray treatment cures in 90% of the instances, and this without operative risk. The following are the reasons given for the superiority of x-ray therapy: it is harmless, and has helped and cured many; there is no operative risk, there is no fear of operation, there is greater likelihood of cure and less likelihood of recurrence, there is likelihood of earlier cure and shorter period of disability, and there is no scar. The author cites DaCosta and the Mayos as surgeons who submit their patients to x-ray therapy prior to operation. In Trostler's experience 4 to 8 full dosage treatments effect the cure. The thymus is also submitted to x-ray treatments in all cases. A note of warning is sounded in the interest of the cautious use of the x-ray, for an agency which is so potent for good is capable

of doing harm when improperly handled (In this paper, the terms Basedow's disease and hyperthyroidism are used synonymously)

—I B

HYPERTHYROIDISM, basal metabolism and radiotherapy Van Allen (H W), J Radiol (Omaha), 1922, 3, 83-85

Hyperthyroidism is a much more common condition than is generally supposed, and in many cases no appreciable enlargement is present even when a plus result is given by the basal metabolism test. Many of these cases are diagnosed as neurasthenia or as disease of the heart muscle. Too much attention has been focused upon "characteristic symptoms" and too little upon the lesser symptoms of nervousness, unusual perspiration, staring eyes with almost entire absence of winking, mental irritability, and slight but gradual loss of weight. The patient may be almost invalidized and only obscure symptoms be present. It is in such cases that the basal metabolism test is invaluable. In treating these cases there is a proper dosage which must be observed or the result will be a failure. The author's technique is $3\frac{1}{2}$ milliamperes, 15 minutes, $4\frac{1}{2}$ mm aluminum filter, $8\frac{1}{2}$ in spark gap, 16 inch distance, 6 treatments on each side of the neck (12 treatments in all) given twice per week. This has been used for years with excellent results. Though a few cases have had to be re-treated, no case has had myxoedema and there have been no deaths. The author believes the basal metabolism test should be given in all cases where a diagnosis of hyperthyroidism is made and in all cases of obscure nervous or suppressed cardio-muscular disease. The test should be given while the patient is in a state of mental quietude and physical rest. The home or the laboratory is a better place than the hospital as a rule because a trip to the hospital is for most people a cause of at least some degree of excitement and nervous strain. After the first test no further one is required until at least a month after the last treatment has been given, the pulse is relied upon to indicate changes in the condition. Charts are shown to illustrate the accuracy of the pulse as an indication of the effect of treatment—Abst, J Radiol, 3, 112

(THYROID) The pathology of toxic and nontoxic adenomatous goiters. Wilson (L B), Tr Ass Am Physicians, 1922, abst J Am M Ass (Chicago), 1922, 78, 1918-1919

True exophthalmic goiter can be divided into three stages (1) early stage, with moderate increase in basal metabolism, often moderate exophthalmos, moderate enlargement, moderate hyperplasia, and diffuse hyperemia of the gland, (2) advanced stage, with high metabolic rate, marked exophthalmos, marked nervous syndrome, marked thyroid enlargement, advanced hyperplasia, diffuse hyperemia, but little if any stored colloid, and (3) the late stage, with high, but sometimes declining metabolic rate, marked nervous syn-

drome, but there is now marked colloid storage, with less hyperemia. The gland is not nodular. Distinct from this picture is a slowly developing type, with increased metabolic rate, but no ocular change, and very frequently associated with nodular thyroids. This, Plummer has called hyperfunctioning adenoma. An effort has been made to determine the difference between the two groups of cases, and to sort patients with symptoms from those without. Two groups at the extremes of the metabolic series have been chosen. Group A included patients with enlarged nodular thyroids, with symptoms of hyperthyroidism, but no exophthalmos, no nervous syndrome, with metabolic rate 20 or more above normal. Group B included patients with enlarged nodular thyroids, without hyperthyroid symptomatology and with metabolism rates within 10 points of normal. About 250 thyroids in each series were studied microscopically. Group A cases showed parenchymal cell hypertrophy with some colloid storage. Grossly the glands are (a) diffuse colloid without new follicle formation, or (b) colloid with new follicle but no capsule formation, or (c) definitely encapsulated areas. These are all of moderate degree. These cases differ in kind and in degree from true exophthalmic goiter. The colloid is passing into the circulation from the parenchymal cells. The parenchymal cells are not under high functional pressure, discharging secretion directly into the vessels. In the new follicle-forming type, we cannot find evidence that this is the essential factor in hyperthyroid symptoms, as even when this picture predominates, there are many areas of colloid absorption by reactivated parenchymal cells. Group B showed no evidence of cell hypertrophy or hyperplasia. The cases could be divided more or less into three groups paralleling those of glands from the hypertrophic series. A few were proliferating adenomas. Disturbance of metabolic rate is the true index of hypothyroidism and hyperthyroidism. Thus the hypertrophic and hyperplastic cells in Group A are responsible for increased metabolic rate, while in Group B there is no substance secreted sufficiently to increase metabolism. One can consider the hypothesis then that symptoms of nonexophthalmic hyperthyroidism are caused by absorption of complete thyroxin secreted in previously stored colloid, but more slowly than in exophthalmic goiter. Stored colloid does contain thyroxin, and the colloid is transmitted from the follicles to the circulation. In true exophthalmic goiter the symptoms may be caused by incompletely elaborated thyroid secretion. This harmonizes with many clinical findings. However, it may be discovered that the disease, true exophthalmic goiter, is primarily a lesion of the nervous system, and that thyroid hyperfunction is a secondary development.—Quoted

(THYROID) Sexual status in sporadic cretinism (Zur Frage der Sexualität bei sporadischem Kretinismus) Wollenberg (H. W.), Med. Klin. (Berl. & Wien), 1922, 18, 144

Short report of a female cretin (infantile myxedema) who at the age of 8 years could not run or speak properly and who had the growth of about a 2 year old child. She is now 28 years old, 130 cm high, but with well developed external female characteristics. Menstrual periods have been regular since 18 years of age and are not modified by cessation of treatment with thyroid tablets, which were taken daily for a period of 12 years. She has been pregnant three times since 1919 —A T R

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